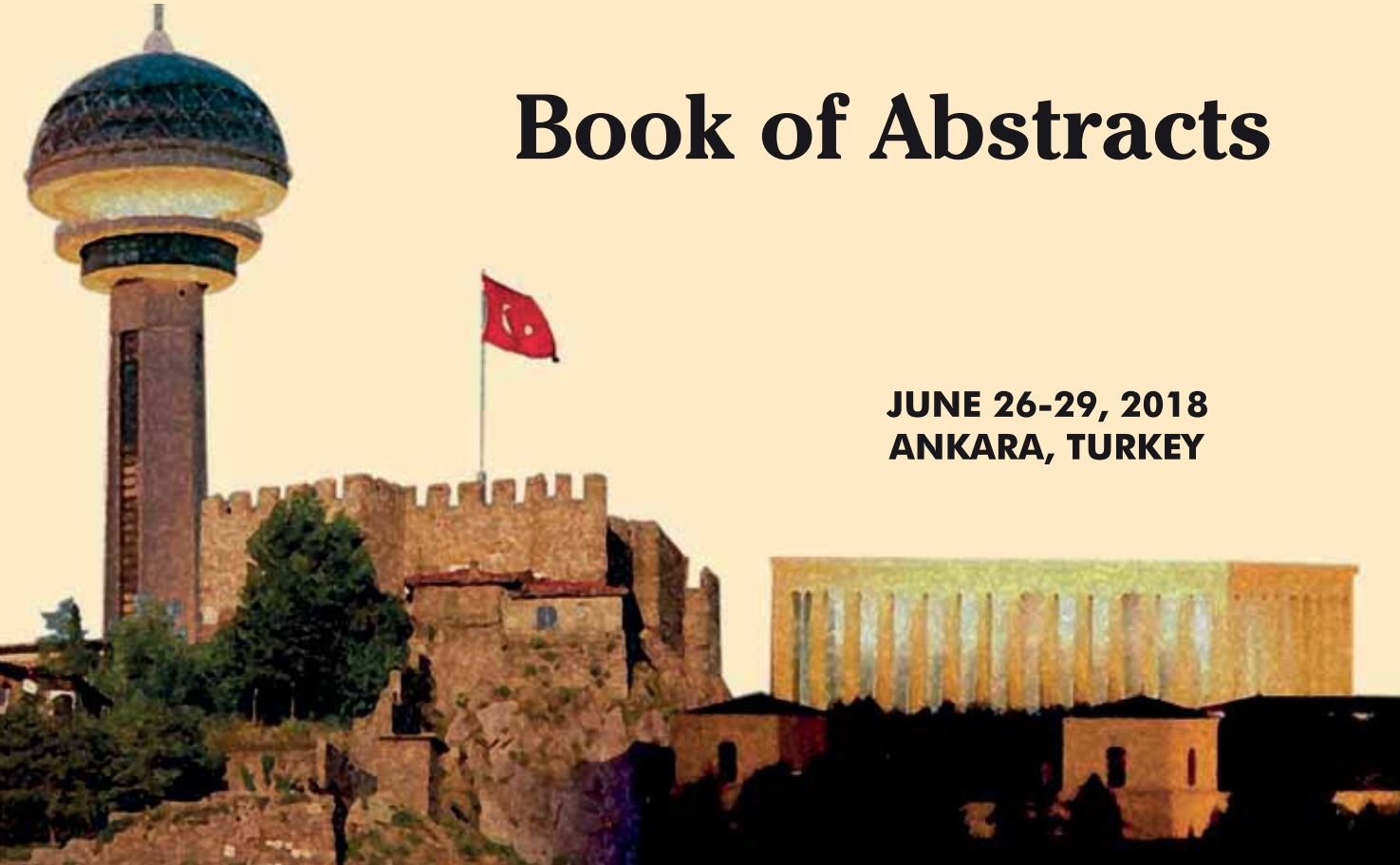
ANKARA UNIVERSITY
FACULTY OF PHARMACY

ISOPS 12th International SYMPOSIUM ON PHARMACEUTICAL SCIENCES



Book of Abstracts

JUNE 26-29, 2018
ANKARA, TURKEY

Ankara University Faculty of Pharmacy Publication No:121

ANKARA UNIVERSITY
FACULTY OF PHARMACY

ISOPS 12th International SYMPOSIUM ON PHARMACEUTICAL SCIENCES

Book of Abstracts

JUNE 26-29, 2018
ANKARA, TURKEY

Book of Abstracts
Ankara University Faculty of Pharmacy Publication No:121
June 2018 Ankara, Turkey

ISBN: 978-975-136-378-3

Basım Başak Matbaacılık ve Tanıtım Hiz. Ltd. Şti.
T: 0312 397 16 17 F: 0312 397 03 07

JUNE 26-29, 2018
ANKARA – TURKEY

ISOPS-12 HAS BEEN GENEROUSLY SUPPORTED BY

1. ANKARA UNIVERSITY
2. THE SCIENTIFIC AND TECHNOLOGICAL RESEARCH COUNCIL OF TURKEY (TUBITAK)
3. TURKISH COOPERATION AND COORDINATION AGENCY (TIKA)
4. REPUBLIC OF TURKEY, MINISTRY OF CULTURE AND TOURISM
5. SELÇUK ECZA DEPOSU TİC. VE SAN. A.Ş.
6. HERBAMED VİTAL SAN. VE TİC. A.Ş.
7. ABDİ İBRAHİM İLAÇ SAN. VE TİC. A.Ş.
8. PHARMACTIVE İLAÇ SAN. VE TİC. A.Ş.
9. GEN İLAÇ VE SAĞLİK ÜRÜNLERİ SAN. VE TİC. A.Ş.
10. NOBEL İLAÇ SAN. VE TİC. A.Ş.
11. ECZACIBAŞI İLAÇ PAZARLAMA A.Ş.
12. İSTANBUL ECZACILAR ÜRETİM TEMİN DAĞITIM KOOPERATİFİ (İSKOOP)
13. TURKISH PHARMACISTS' ASSOCIATION (TEB)
14. BURSA ECZACILAR ÜRETİM TEMİN VE DAĞITIM KOOPERATİFİ (BEK)
15. BERKO İLAÇ VE KİMYA SAN. A.Ş.
16. BİEM İLAÇ SAN. VE TİC. A.Ş.
17. PHARMACISTS' CHAMBER OF ANKARA
18. PHARMACISTS' CHAMBER OF TRABZON
19. PHARMACISTS' CHAMBER OF IZMIR
20. PHARMACISTS' CHAMBER OF ISTANBUL
21. LİBA LABORATUARLARI A.Ş.
22. 4D SİSTEM TİC. LTD. ŞTİ.
23. DROGSAN İLAÇLARI SAN. VE TİC. A.Ş.
24. CENTURION PHARMA İLAÇ SAN. VE.
25. RECORDATİ İLAÇ VE HAMMADDELERİ SAN. VE TİC. A.Ş.
26. MERCK SD- ISPOR
27. KEÇİÖREN MUNICIPALITY
28. ARVEN İLAÇ SAN. VE TİC. A.Ş.
29. PHENOMENEX INC.
30. AMGEN İLAÇ TİC. LTD. ŞTİ.
31. AYES GROUP
32. SANOVEL İLAÇ SAN. VE TİC. A.Ş.
33. BİOVALDA SAĞLIK TEKNOLOJİLERİ EĞİTİM ARAŞTIRMA SANAYİ TİCARET A. Ş.
34. CİNNAGEN İLAÇ SAN. VE TİC. A.Ş.

Dear Participants and Guests,

I would like to thank all the participants of 12th International Symposium on Pharmaceutical Sciences for their valuable contributions. You had spent your days in a charming country that shelters the oldest and the greatiest cultures and civilizations of the world.

The development of Symposiums on Pharmaceutical Sciences, which is held in our faculty, is getting more expanded through the 1989. This symposium was organized bianually until 1997 and then every three years. The previous 11 symposiums were held as;

1st International Symposium on Pharmaceutical Sciences	21-23 June 1989
2nd International Symposium on Pharmaceutical Sciences	11-14 June 1991
3rd International Symposium on Pharmaceutical Sciences	15-18 June 1993
4th International Symposium on Pharmaceutical Sciences	27-30 June 1995
5th International Symposium on Pharmaceutical Sciences	24-27 June 1997
6th International Symposium on Pharmaceutical Sciences	27-29 June 2000
7th International Symposium on Pharmaceutical Sciences	24-27 June 2003
8th International Symposium on Pharmaceutical Sciences	13-16 June 2006
9th International Symposium on Pharmaceutical Sciences	23-26 June 2009
10th International Symposium on Pharmaceutical Sciences	26-29 June 2012
11th International Symposium on Pharmaceutical Sciences	9-12 June 2015

The second institution in pharmacy education, Faculty of Pharmacy of Ankara University was founded in 1960 and started education in 1961-1962 semester. The length of pharmacy education had been 4 years until 2005 and increased to 5 years starting by that date. The new 5-year educational program has been updated according to the suggestions of the Advisory Committee on Pharmaceutical Training. This new program covers the basic courses such as mathematics, physics, chemistry as well as the basics in pharmacy education. Fifth year consists of some elective courses and the preparation of a graduation project. During the 5 years, students have to complete the 6-month training program mandatory in pharmacy/hospital or optionally in the industry. Our faculty has 6904 graduates since the established and the current number of students is 967.

Present educational and scientific resources allow a total of 138 faculty members, 49 professors, 13 associate professors, 16 assistant professors, 60 research assistants in our faculty. Moreover, 66 administrative staff members and other personnel are working at different offices.

The mission of 12th International Symposium of Pharmaceutical Sciences was to perform a broad scientific perspective by the invitation of distinguished scientists having national / international reputation in their areas, so most recent advances were discussed interactively and empower the knowledge-based drug research development and multidiciplinary collaborations. It was our intention to make this symposium a memorable event, both scientifically and socially for the attendees.

We are pleased to announce that around 800 scientists were registered to ISOPS-12 in which 664 oral/poster presentations participated as well as 41 distinguished lecturers invited from several countries.

In addition to general sessions and the posters, the exhibitors of some companies from drug industry that had introduced their equipments and products.

The topic of the Panel was “The road to the strong Turkish Pharmaceutical Industry”. The lecturers were: Dr Hakkı Gürsöz, Prof.Dr.Nurten Özdemir, Ali Alkan, Turgut Tokgöz, Kemalettin Akalın, Ümit Dereli, Fatma Taman.

On the behalf of the Organizing Committee, I would like to mention my gratitude to the President of Ankara University who gave the whole support for the Symposium Organization. I would like to thank Turkish Ministry of Culture, Turkish Cooperation and coordination Agency, The Scientific and Technological Research Council of Turkey (TUBITAK), Turkish Pharmacist's Association and Pharmacist's Chamber of Ankara, Trabzon, İzmir, İstanbul and valuable represents of the pharmaceutical industry for their financial supports and pharmaceutical companies for their valuable sponsorship. I congratulate the organizing committee and all the other committees with all my heart and also all academic and managing personnel because of their extensive work. .

Prof. Dr. Gülbin ÖZÇELİKAY

Chair of ISOPS-12

Honory President of the Symposium

Prof. Dr. Erkan İBİŞ

President of Ankara University

ORGANIZING COMMITTEE

Gülbin ÖZÇELİKAY (Chair)
Bengi USLU (Secretariat)
Ebru ARIOĞLU İNAN
Sinem ASLAN ERDEM
Zeynep ATEŞ ALAGÖZ
Filiz BAKAR ATEŞ
Meltem CEYLAN ÜNLÜSOY
Gizem GÜLPINAR
Ceyda Sibel KILIÇ
Müge KILIÇARSLAN
Işıl ÖZAKÇA
Zerrin SEZGİN BAYINDIR
Aylin ÜSTÜNDAĞ
Müjde YÜCE ERYILMAZ

SOCIAL COMMITTEE

Miray ARSLAN
Kayhan BOLELLİ
Merve DEMİRBÜGEN
Gülnur EKŞİ
Cem ERKMEN
Melek KARACAOĞLU
Ecem KAYA
Merve Eylül KIYMACI
Sevinç KURBANOĞLU
Işıl ÖZAKÇA
Göksu ÖZÇELİKAY
Ceyda Tuba ŞENGEL TÜRK

SCIENTIFIC COMMITTEE

Dilek AK (Turkey)
Mehmet ALP (Turkey)
Nurten ALTANLAR (Turkey)
İlker ATEŞ (Turkey)
Özlem BAHADIR ACIKARA
Rudolf BAUER (Austria)
Arzu BEŞİKCİ (Turkey)
Zeliha BÜYÜKBİNGÖL (Turkey)
Afonso Miguel Neves CAVACO (Portugal)
Bezhan CHANKVATADZE (Georgia)
Paolo COLOMBO (Italy)
Ursula GROHMANN (Italy)
Zuhal GÜVENALP (Turkey)
Nilgün KARALI (Turkey)
Ceyda Sibel KILIÇ (Turkey)
Alf LAMPRECHT (Germany)
Vesna MATOVIC (Serbia)
Nurten ÖZDEMİR (Turkey)
Özgen ÖZER (Turkey)
Marco RADI (Italy)
Satyajit SARKER (UK)
Luciano SASO (Italy)
Robert SINDELAR (Canada)
Claudiu T. SUPURAN (Italy)
Sinan SÜZEN (Turkey)
Sevgi ŞAR (Turkey)
Zühre ŞENTÜRK (Turkey)
Meral TORUN (Turkey)
Selen YEĞENOĞLU (Turkey)
Sulhiye YILDIZ (Turkey)
Antonio ZAZA (Italy)

CONTENTS

PLENARY LECTURES

ORAL PRESENTATIONS

POSTER PRESENTATIONS

PLENARY LECTURES

PL-1: QUICK, EASY, CHEAP, EFFECTIVE, RUGGED, AND SAFE "QUECHERS" SAMPLE PREPARATION APPROACH FOR RESIDUE ANALYSIS USING TRADITIONAL DETECTORS IN CHROMATOGRAPHY

EL-ATY, A.

Department of Veterinary Pharmacology and Toxicology, College of Veterinary Medicine, Konkuk University, Seoul, Republic of Korea

Department of Pharmacology, Faculty of Veterinary Medicine, Cairo University, Giza, Egypt

In residue analysis, relatively low-sensitivity traditional detectors, such as UV, diode array, electron-capture, flame photometric, and nitrogen-phosphorus detectors, have been used following classical sample preparation (liquid-liquid extraction and open glass column cleanup); however, the extraction method is laborious, time-consuming, and requires large volumes of toxic organic solvents. A quick, easy, cheap, effective, rugged, and safe method was introduced in 2003 and coupled with selective and sensitive mass detectors to overcome the aforementioned drawbacks. Compared to traditional detectors, mass spectrometers are still far more expensive and not available in most modestly equipped laboratories, owing to maintenance and cost-related issues. Even available, traditional detectors are still being used for analysis of residues in agricultural commodities. It is widely known that the quick, easy, cheap, effective, rugged, and safe method is incompatible with conventional detectors owing to matrix complexity and low sensitivity. Therefore, modifications using column/cartridge-based solid-phase extraction instead of dispersive solid-phase extraction for cleanup have been applied in most cases to compensate and enable the adaptation of the extraction method to conventional detectors. In gas chromatography, the matrix enhancement effect of some analytes has been observed, which lowers the limit of detection and, therefore, enables gas chromatography to be compatible with the quick, easy, cheap, effective, rugged, and safe extraction method. For liquid chromatography with a UV detector, a combination of column/cartridge-based solid-phase extraction and dispersive solid-phase extraction was found to reduce the matrix interference and increase the sensitivity. A suitable double-layer column/cartridge-based solid-phase extraction might be the perfect solution, instead of a time-consuming combination of column/cartridge-based solid-phase extraction and dispersive solid-phase extraction. Therefore, replacing dispersive solid-phase extraction with column/cartridge-based solid-phase extraction in the cleanup step can make the quick, easy, cheap, effective, rugged, and safe extraction method compatible with traditional detectors for more sensitive, effective, and green analysis.

PL-2: COULD STRESSED PLANTS HEAL STRESSED MANKIND? ROLE OF PLANT STRESS IN BIOACTIVE NATURAL PRODUCT BIOSYNTHESIS

[1,2] Matkowski, A., [1] Zielińska, S., [3] Libik-Konieczny,M., [4] Konieczny, R., [1] Kozłowska, W., [2] Jaśpińska,J., [2,5] Pawlikowska, A., [1,6] Ślusarczyk, S.

[1]Dept. Pharmaceutical Biology and Botany, Medical University in Wroclaw, Poland;

[2]Botanical Garden of Medicinal Plants, Wroclaw Medical University, Poland;

[3]Dept. Stress Biology, Institute of Plant Physiology, Polish Academy of Science, Krakow, Poland;

4Dept. Plant Cytology and Embryology, Jagiellonian University, Krakow, Poland;

5Dept. Horticulture, Wroclaw University of Life Sciences, Poland

6Dept. Biochemistry and Crop Quality, IUNG-Institute of Plant Cultivation and Soil Science, Pulawy, Poland.

An imbalance between the reactive oxygen species (ROS) production and antioxidant defense leads to oxidative stress in a plant organism. The paradox of aerobic life is that organisms cannot exist without oxygen though oxygen is dangerous to their existence. Oxygen serves as a terminal electron acceptor during cellular respiration, which provides a high yield of energy. In green plants, oxygen and oxidating molecules are generated during photosynthesis. One of the most important evolutionary achievement of higher eukaryotic aerobic organisms is that they can cope with "double-edge sword" – the oxygen molecule. All aerobic organisms are equipped with a redox regulation system (antioxidant system) that can keep ROS level at the physiological concentration required for normal cellular functions. ROS have dual role that depend upon their concentration in the cell. Thus, the role of antioxidant systems is not to remove oxidants entirely, but of keeping them at an optimum level. ROS can serve as intra-, and intercellular messengers in physiological processes such as the activation of cell signaling cascades, gene expression or apoptosis. The accumulation of ROS in response to biotic and abiotic stress can cause the metabolic changes and physiological damage of plant cell despite the activity of efficient antioxidant systems. Plant organisms being devoid of motility and immune system have elaborated strategies resting on synthesis of variety of secondary metabolites playing important function in defense against oxidative stress. Plant-derived antioxidant compounds may be able to bolster significantly biological resistance against oxidants in animal cells. In the last decades, secondary metabolites became a subject of increasing interest relevant to their significant practical implication for medicinal, nutritive

and cosmetic purposes. The entire category of herbal adaptogens is considered as essential to improving the quality of life in the hectic modern societies. Plant antioxidants, such as flavonoids, carotenoids, tocopherols, betalains, resveratrol, rosmarinic acid, and other are involved in a set of reactions to protect cell functions. For instance, chelation of transition metals by flavonoids that interferes with the generation of reactive oxygen species (ROS), thus contributing to a powerful antioxidant/antiradical performance. The presence of conjugated double bonds (delocalized π-electrons) in flavonoids (including anthocyanins), hydroxycinnamic acids and xanthophylls predispose them to photoprotective function.

In our research program, we employ various experimental systems, reaching from conventional field cultivation, through hydroponics and *in vitro* cell, tissue and organ culture of medicinal plants. We use several non-model species of Asian origin and their European relatives. The metabolic profiles of plants or *in vitro* cultures challenged by stress factors are monitored by targeted metabolomic approach using hyphenated chromatography-spectroscopy techniques as well as qNMR followed by multivariate statistics. In conclusion, results of many advanced experiments on the oxidative stress responses in plants support the hypothesis that the trade-off between growth and defense in plant cells exist, and that it is mediated by the resources availability. In that way, plant important antioxidants production is orchestrated by the regulation mechanisms of plant response to environmental conditions. These mechanism can be exploited by humans in form of improving medicinal properties of herbs, especially those that are known as adaptogens.

PL-3: CLINICAL COMMUNICATION SKILLS: DOES IT REALLY MATTER IN PHARMACY PRACTICE

Cavaco, A.M.

Pharmacy practice encompasses a number of professional activities, usually associated with medicines usage by patients. These pharmacists' duties comprise the optimization of the clinical effectiveness and safety of medicines taken by patients. To be able to manage pharmacotherapy and evaluate its success with each patient, pharmacists need to collect and provide information. The individual patient is the main source of information, both objective and subjective. However, patients are more than data providers. Human nature is complex, suggesting the use of proper clinical interviewing skills. Although widely recognized as a key element in healthcare, clinical communication skills are usually less covered in pharmacy education and research. This presentation aims to address and debate how communication skills are essential to take full advantage of the existing pharmaceutical knowledge i.e. to achieve the aim of translating science into pharmacy practice, and care for persons with health conditions.

PL-4: MICRONUTRIENT PROFILING IN FOOD AND BIOLOGICAL SAMPLES: STRATEGIES FOR TARGETED AND UNTARGETED ANALYSIS OF VITAMINS AND CAROTENOIDS.

Gentili, A., Tomai, P., Dal Bosco, C.,Curini, R.

La Sapienza University, Department of Chemistry, Rome, Italy.

Elucidation of natural distribution of vitamins and carotenoids is a challenging and quite non-trivial analytical task. The difficulties in large scale profiling of fat-soluble micronutrients as well as in speciation of homologues belonging to the same vitamin group are numerous and occur at different levels of the analytical procedure. They can arise from the commercial unavailability and/or cost of authentic standards, large number of forms, definition of common analysis conditions, chemical instability, creation of artefacts and occurrence of isomers. Our research team has a ten-year experience in this field and has developed effective approaches to solve the above-mentioned difficulties [1-5]. Extraction procedures have been developed to preserve vitamins in their natural forms and to easily discriminate between free and esterified forms. Non-aqueous reversed phase conditions have been studied to be compatible with APCI-MS detection and to obtain an effective chromatographic resolution. UV/Vis-MS parameters have been individuated to quickly distinguish structural isomers and related families of geometrical isomers. Aim of this communication is: i) to shortly review the importance of vitamins for human health, ii) illustrate the potential of liquid chromatography- diode array detector/quadrupole linear ion trap hyphenation for the targeted and untargeted analysis of vitamins and carotenoids in food and biological samples and iii) report some examples of practical applications.

REFERENCES:

1. Gentili A. et alt. (2008). Rapid Communications in Mass Spectrometry, 22:2029-2043.
2. Gentili A., Caretti, F. (2011). Journal of Chromatography A, 1218:684-697.
3. Gentili A. et alt. (2012). Journal of Agricultural and Food Chemistry, 61:1628-1639.
4. Gentili, A. et alt. (2015). Journal of Agricultural and Food Chemistry, 63:7428-7439.
5. Rocchi S., et alt. (2016). Food Chemistry, 211:455-464.

PL-5: APPLICATION OF TEXT MINING APPROACHES TO DRUG DISCOVERY

Tropsha, A.

K.H. Lee Distinguished Professor

Associate Dean for Pharmacoinformatics and Data Science

UNC Eshelman School of Pharmacy

UNC Chapel Hill

UNC Chapel Hill, NC [2]7599, USA

Text mining approaches find growing application in disciplines as diverse as health care analytics and politics. I will discuss applications of text mining to areas of interest to drug discovery including prediction of drug side effects, drug repurposing, and establishing clinical outcomes pathways for therapeutic effects of drugs. I will discuss the use of diverse sources of knowledge to enable the above applications such as social media and biomedical literature. Finally, I will discuss the unique application of text mining concepts combined with artificial intelligence approaches to the difficult task of designing new chemical libraries with the desired properties. In this proof-of-concept study, we have employed an integrative strategy to design chemical libraries biased toward compounds with either maximal, minimal, or specific ranges of physical properties, such as melting point and hydrophobicity, as well as to develop novel putative inhibitors of JAK2. The approach that I will discuss can find general use for generating targeted chemical libraries optimized for a single desired property or multiple properties.

REFERENCES

1. Tropsha, A. Uncommon Data Sources for QSAR Modeling. In: Applied Chemoinformatics: Achievements and Future Opportunities. T. Engel and J. Gasteiger, Eds., 2018, Wiley-VCH Verlag GmbH & Co (in press).
2. Baker NC, Ekins S, Williams AJ, Tropsha A. A bibliometric review of drug repurposing. Drug Discov Today, 2018, pii: S1359-6446(17)30287-8. doi: 10.1016/j.drudis.2018.01.018
3. Popova, M., Isayev, O., and Tropsha, A. Deep Reinforcement Learning for De-Novo Drug Design, 2017, https://arxiv.org/abs/1711.10907
4. Miftahutdinov, Z., Tutubalina, E., Tropsha, A. Identifying disease-related expressions in reviews using conditional random fields. Komp'juternaja Lingvistika i Intellektual'nye Tehnologii, 2017, 1 (16), 155-166

PL-6: WHEN EXCIPIENTS BECOME THE ACTIVE – NEW DRUG DELIVERY STRATEGIES IN CANCER AND ANTI-INFLAMMATORY THERAPY

Lamprecht, A.

University of Bonn, Department of Pharmaceutics, Bonn, Germany

Pharmaceutical excipients possess a great variety of physicochemical functions in dosage forms, mainly based on the prerequisite to be inert against other formulation components as well as being inactive from pharmacologic point of view. However, in recent years more and more studies appear in the literature highlighting certain therapeutic benefits from such "inert" excipients. This presentation will focus on the use of several examples where a clear therapeutic effect is btained from the sole excipient.

Chitosan, with initial intention to formulate a bioadhesive dosage form for a better therapy of inflammatory bowel disease showed signifcant anti-inflammatory effects itself (1). Similarly, other natural polymers showed an anti-inflammatory effect without the need of the additional use of an anti-inflammatory drug (2).

Another aspect is the pharmacological activity of excipients providing inhibitory effects on multidrug resistance phenomena in cancer therapy. The use of certain amphiphilic components in a drug formulation help to increase the intracellular level of cytotoxic drugs, turning into a more efficient therapy (3).

Finally, a very recent discovery is the use of approved pharmaceutical excipients for efficient cancer immune therapy (4). Cargo-free nanoparticles allow to reactivate the immune system against a xenograft tumor in mice leading to full remission in about 25% of the case and also providing a memory effect which potentially is beneficial to prevent recurrencies.

REFERENCES:

1. Bautzová T, Rabišková M, Béduneau A, Pellequer Y, Lamprecht A. (2012) Eur J Pharm Biopharm., 81:379-85.
2. Okunlola A, Odeku OA, Lamprecht A, Oyagbemi AA, Oridupa OA, Aina OO. (2015) Int J Biol Macromol., 79:226-34.
3. Singh MS, Lamprecht A. (2016) Drug Dev Ind Pharm., 42:325-31.
4. Shetab Boushehri MA, Stein V, Lamprecht A. (2018) Biomaterials, 166:1-12.
5. Niebel W, Walkenbach K, Béduneau A, Pellequer Y, Lamprecht A. (2012) J Control Release, 160:659-65

PL-7: DIAGNOSTICS USING PAPER-BASED PLATFORMS

Merkoci, A.

Catalan Institute of Nanoscience and Nanotechnology (ICN2), CSIC and The Barcelona Institute of Science and Technology, Campus UAB, Bellaterra, 0819[3] Barcelona, Spain.

ICREA - Institucio Catalana de Recerca i Estudis Avançats, 080[1]0 Barcelona, Spain.

Biosensors field is progressing rapidly and the demand for cost efficient platforms is the key factor for their success. Physical, chemical and mechanical properties of cellulose in both micro and nanofiber-based networks combined with their abundance in nature or easy to prepare and control procedures are making these materials of great interest while looking for cost-efficient and green alternatives for device production technologies. Both paper and nanopaper-based biosensors are emerging as a new class of devices with the objective to fulfil the “World Health Organization” requisites to be ASSURED: affordable, sensitive, specific, user-friendly, rapid and robust, equipment free and deliverable to end-users. How to design simple paper-based biosensor architectures? How to tune their analytical performance upon demand? How one can ‘marriage’ nanomaterials such as metallic nanoparticles, quantum dots and even graphene with paper and what is the benefit? How we can make these devices more robust, sensitive and with multiplexing capabilities? Can we bring these low cost and efficient devices to places with low resources, extreme conditions or even at our homes? Which are the perspectives to link these simple platforms and detection technologies with mobile phone communication? I will try to give responses to these questions through various interesting applications related to protein, DNA and even contaminants detection all of extreme importance for diagnostics, environment control, safety and security.

REFERENCES:

1. C. Parolo, A. Merkoçi, “Paper based nanobiosensors for diagnostics”, Chem. Soc. Rev., 42, 2013, 450-457 ;
2. D. Quesada-González, A. Merkoçi. « Nanoparticle-based lateral flow biosensors », Biosensors and Bioelectronics, 73, 2015, 47–63 ;
3. E. Morales-Narváez, H.Golmohammadi, T. Naghdi, H. Yousefi, U. Kostiv, D. Horak, N. Pourreza, A.Merkoçi. “Nanopaper as an optical sensing platform “, ACS Nano, 9, 2015, 7296-7305 ;
4. E. Morales-Narvaez, T. Naghdi, E. Zor, A. Merkoci, “Photoluminescent Lateral-Flow Immunoassay Revealed by Graphene Oxide: Highly Sensitive Paper-Based Pathogen Detection”, Anal. Chem. 2015, 87, 8573−8577.
5. L. Baptista-Pires, C. C. Mayorga-Martínez, M.M. Sanchez, H. Monton, A. Merkoçi, “Water Activated Graphene Oxide Transfer Using Wax Printed Membranes for Fast Patterning of a Touch Sensitive Device”, ACS Nano 2016, 10, 853−860
6. A.M. López_Marzo, A. Merkoçi, “Paper-based sensors and assays: a success of the engineering design and the convergence of knowledge areas”, Lab Chip, 2016, 16, 3150–3176
7. E.Morales-Narváez, L. Baptista-Pires, A. Zamora-Gálvez, A. Merkoçi, “Graphene-based biosensors: Going simple”, Advanced Materials, 2017, 29, 1604905.

PL-8: PEARLS AND PITFALLS OF CLINICAL PHARMACY IN TURKEY

Bayraktar-Ekincioglu, A

Hacettepe University, Faculty of Pharmacy, Department of Clinical Pharmacy, Ankara-Turkey

Clinical pharmacy has received increasing attention of healthcare professionals in the view of pharmacy practice over 15 years in Turkey. As a health science discipline, clinical pharmacy aims to optimise drug therapy, promotes health and prevents diseases where a patient is the focus of provision of pharmaceutical care. Pharmaceutical care is defined as ‘responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient’s quality of life’. Clinical pharmacists are responsible of provision of pharmaceutical care in collaboration with other healthcare professionals.

Since the pharmacy has gone through many changes as a profession, the practice of pharmacy evolved according to the needs and regulations of the countries. In Turkey, the concept has been introduced into the pharmacy area at the end of 1990s and it became well-known and accepted by the 2000s. Although there has been debates about the terms ‘clinical pharmacy / pharmacist’, ‘hospital pharmacist’ and ‘clinical pharmacology’ at the beginning, the concept is well-understood and appreciated amongst pharmacists as well as other healthcare professionals by now. A widespread implementation of clinical pharmacy is expanded by the active involvement of postgraduate pharmacy students and the establishment of the Residency Programme in Clinical Pharmacy in 2016 and the National Residency Exam in 2017.

According to the statistics of the Ministry of Health, there are about 35.000 pharmacists in Turkey, of those 90% work in the community and approximately 6% employed in the hospitals. In regards to increasing number of graduated pharmacists from the faculties each year and regulations on limitations in the number of pharmacies per population, new areas for practice of pharmacy have been discussed and specialization

in clinical pharmacy appeared as solution for the profession's obstacle.

Although the concept of clinical pharmacy, implications in practice and its outcomes in healthcare services are having great attention of pharmacists as well as legislative authorities in Turkey; clinical pharmacist's authority, responsibilities and professional statutory rights should be clearly defined and qualified specialized pharmacists should be designated in relevant institutions according to the requirements of healthcare system.

Furthermore, there is still a need for many research studies at national level that focus on the impact of clinical pharmacy on health-related outcomes. The outcomes related with patient and disease management, drug usage and utilization of healthcare services should be manifested precisely and the results shared with other healthcare professionals and legislative authorities.

PL-9: RECENT DEVELOPMENTS IN ENANTIOSEPARATION OF CHIRAL DRUGS BY USING CAPILLARY ELECTROPHORESIS

Chankvetadze, B.

Institute of Physical and Analytical Chemistry, School of Exact and Natural Sciences, Tbilisi State University, Chavchavadze Ave [3], Tbilisi 0179, Georgia.

INTRODUCTION:

Capillary electrophoresis (CE) is very useful technique for analytical scale separation of enantiomers. It is clear that even only at the expense of higher peak efficiency CE may allow to observe enantioseparation for certain chiral analyte-selector pairs where the separation power of HPLC is insufficient for achieving this goal. In addition, chiral CE offers almost unlimited possibility from the viewpoint of adjustment of separation factor. Together with aforementioned conceptual advantages CE offers some favorable technical characteristics for achieving high separation selectivity. Chiral CE is a powerful technique not only for separation of enantiomers but also for understanding fine mechanisms of enantioselective selector-selectand interactions. However, in order to achieve this goal CE must be used in combination with other instrumental (for instance, nuclear magnetic resonance spectroscopy) and calculation (molecular modeling, molecular mechanics) techniques.

MATERIALS AND METHODS:

The results included in this presentation were obtained by using CE, various methods of nuclear magnetic resonance (NMR) spectroscopy and molecular modeling/molecular mechanics (MM) calculations.

RESULTS:

Our recent results on separation mechanisms of some chiral drugs, such as enilconazole, clenpenterol and terbutaline will be used in order to illustrate the power of the combination of CE, NMR spectroscopy and MM calculations for better understanding of noncovalent intermolecular interactions between chiral drugs and cyclodextrins [1, 2].

CONCLUSIONS:

This presentation illustrates the power of the combined use of CE, nuclear magnetic resonance spectroscopy and molecular modeling calculations for separation of enantiomers of chiral drugs, as well as for understanding of chiral recognition mechanisms of cyclodextrins.

ACKNOWLEDGEMENTS:

This project was supported financially in part by the Rustaveli National Science Foundation (RNSF) of Georgia (Project No. 217642).

REFERENCES:

1. Gogolashvili A, Tatunashvili E, Chankvetadze L, Sohajda T, Szeman J, Salgado A, Chankvetadze B, (2017). Electrophoresis, 38:1851-1859.
2. A. Salgado, Tatunashvili E, Gogolashvili A, Gago F, Chankvetadze B, (2017). Physical Chemistry & Chemical Physics, 19:27935-27939.

PL-10: DEVELOPMENT OF NOVEL TARGETED THERAPIES FOR BREAST CANCERS

Ozpolat, B

Currently breast cancer is most commonly diagnosed cancer in women. Triple negative breast cancer (TNBC) is the most aggressive subtype of breast cancer and associated with poor patient survival and high mortality rates. Due to highly heterogeneous genetic feature of the diseases has prevented identification of therapeutic targets and development of targeted therapies for TNBC . We recently discovered that eEF-2 Kinase (eEF2K) is highly overexpressed in TNBC patients and its expression is associated with significantly shooter patient survival. Using in vitro and in vivo tumor models in mice, we demonstrated that eEF2K promotes cell proliferation, invasion, metastasis and tumorigenesis. We also developed siRNA, microRNA-based therapeutics and demonstrated for the first time that in vivo targeting of this previously untargeted kinase by systemic administration inhibits tumor growth in several preclinical TNBC tumor xenograft models. The talk will also give background in targeted therapies used in cancer patients and our novel targeted therapies.

PL-11: NOVEL PROSPECTIVES FOR ORGANOSELENIUM COMPOUNDS IN MEDICINAL CHEMISTRY.

Santi C.

Group of Catalysis and Organic Green Chemistry Department of Pharmaceutical Sciences University of Perugia

INTRODUCTION:

The biological activity of organoselenium compounds is an attractive topic of research after a long period in which the perception about selenium toxicity strongly limited this of investigations. With the only exception of ebselen, that is the most pharmacologically studied seleniumcontaining compound, several other classes of derivatives were studied in the past almost exclusively as antioxidant and glutathione peroxidase (GPx)-mimicking agents.

RESULTS:

In this context we gave our contribution with the development of a number of selenium derivatives that have been tested, looking beyond the classical concept of antioxidant agents, for their ability to act as antiretrovirals targeting the key HIV protein NCp7 (1), as inhibitors of biofilm formation (2) as hormetic agents activated by mild stressors (3) or as selective enzymatic inhibitors (4). In addition, we developed a simple and versatile procedure for a quick conversion of diselenides into bensoisoselenazolones and non-conventional selenium derivatives were prepared and tested as mimetic of selenoenzymes, in particular glutathione peroxidase and deiodinases. Novel results obtained in the elucidation of the development of small molecules forr the the activation od tyroid hormones will be presented.

ACKNOWLEDGEMENTS:

These studies were performed under the umbrella of the international scinetific network SeSRedCat (Selnium sullfur and Redox Catalysts)

REFERENCES:

1. Sancineto L, Mariotti A, Bagnoli L, Marini F, Desantis J, Iraci N, Santi C, Pannecouque C, Tabarrini O. Design and Synthesis of DiselenoBisBenzamides (DISeBAs) as Nucleocapsid Protein 7 (NCp7) Inhibitors with anti-HIV Activity. Journal of medicinal chemistry 2015; 58(24): 9601-9614.
2. Sancineto, L., Piccioni, M., De Marco, S., Pagiotti, R., Nascimento, V., Braga, A.L., Santi, C., Pietrella, D. Diphenyl diselenide derivatives inhibit microbial biofilm formation involved in wound infection (2016) BMC Microbiology, 16 (1), art. no. 220.
3. Bartolini D, Commodi J, Piroddi M, Incipini L, Sancineto L, Santi C, Galli F. Glutathione Stransferase pi expression regulates the Nrf2-dependent response to hormetic diselenides. Free radical biology & medicine 2015; 88(Pt B): 466-480.
4. Bartolini, D., Piroddi, M., Tidei, C., Giovagnoli, S., Pietrella, D., Manevich, Y., Tew, K.D., Giustarini, D., Rossi, R., Townsend, D.M., Santi, C., Galli, F. Reaction kinetics and targeting to cellular glutathione S-transferase of the glutathione peroxidase mimetic PhSeZnCl and its d,l-polylactide microparticle formulation (2015) Free Radical Biology and Medicine, 78, pp. 56-65.

PL-12: SYNTHESIS AND BIOLOGICAL APPLICATION OF PORPHYRINS

[1] Kurniawan, F., [1] Muhammad, HN.,[2] Arba, M, [1] Tjahjono, DH.

[1] Bandung Institute of Technology, School of Pharmacy, Bandung, Indonesia

[2] Halu Oleo University, Faculty of Pharmacy, Kendari, Indonesia

INTRODUCTION:

Porphyrin derivatives have become increasingly important reagent candidates in analytical chemistry because of its persistent UV-visible spectra as well as large molar absorption coefficient and high stability. It has been reported that porphyrin derivatives interact with DNA (1), and it has telomerase inhibition activity (2). Porphyrins also show a selectivity to melanoma and hepatoma cancer (3).

MATERIALS AND METHODS:

Porphyrin derivatives have been designed and synthesized according to previous method (1,4). The designed cationic porphyrins has been applied to study the interaction model of molecules to double stranded-DNA. The SOD activity of manganese-porphyrin complexes were studied *in silico* as well as *in vitro*. Some porphyrins were also labeled with radionuclide to study their characteristic as ligand for radiopharmaceuticals.

RESULTS:

Based on the change in UV-visible, CD and MCD spectra of cationic porphyrin, and change in viscosity of DNA upon interaction with porphyrin, the binding mode of interaction may be classified as intercalation, outside binding, or outside binding mode with stacking. Electron-withdrawing effects and charge distribution within isomeric imidazolium and pyrazolium derivatives of *meso*-substituent are remarkably different and has high influence on SOD activity. The moiety of porphyrins for labeling process determine labeling efficiency.

CONCLUSIONS:

Porphyrins are versatile molecule to study binding mode of interaction. Imidazoliumylporphyrin has higher SOD activity compare to those of porphyrins with other *meso*-substituents. Porphyrin derivatives show a potential properties as ligand for radiopharmaceutical.

ACKNOWLEDGEMENTS:

This study was supported in part by a grant of Program Riset Multidisiplin ITB 2018.

REFERENCES:

1. Tjahjono DH, Akutsu T, Yoshioka N, Inoue H (1999). Biochim. Biophys. Acta, 1472: 333-343.
2. Kim, M-Y, Gleason-Guzman, M, Izbicka, E, Nishioka, D, Hurley, LH (2003). Cancer Reserach, 63:3247-3256.
3. Jia Z, Deng H, Luo, S (2008), Eur. J. Nucl. Med. Mol. Imaging, 35:734-742.
4. Tjahjono DH, Yamamoto T, Ichimoto S, Yoshioka N, Inoue H (2000). J. Chem. Soc., Perkin Trans. 1, 3077-3081.

PL-13: PHARMACY EDUCATION AND CLINICAL PRACTICE IN THE UNITED STATES

[1] -[2] Hawes, EM.

[1] University of North Carolina Eshelman School of Pharmacy, Chapel Hıll, North Carolina, USA

[2] University of North Carolina Eshelman School of Medicine, Chapel Hıll, North Carolina, USA

In the United States, pharmacists are responsible for the provision of safe, effective, efficient, and accountable medication related-care for patients [1]. The Pharm.D. curriculum consists of education that meets the standards set by the Accreditation Council for Pharmacy Education (ACPE). İn 2016, ACPE released updated curriculum standards in order to incorporate advances in real-world pharmacy practice with more emphasis on patient-centered care, multidiscplinary teams, evidence-based practice, quality improvement, and information technology [2]. Pharmacist education, post-graduate training, and practice models closely mimics those of physicians. Advanced training, in addition to credentialing, privileging, and collaborative practice agreements have placed pharmacists in a position to serve as stewards of the medication use process, champions of patient safety, and critical contributors to optimal clinical outcomes [3].

1. American Society of Health-System Pharmacists. The consensus of the pharmacy practice model summit. Am J Health-Syst Pharm. 2011;68:1148–52.
2. Accreditation Council for Pharmacy Education. Accreditation Standards and Key Elements for the Professional Program in Pharmacy Leading to the Doctor of Pharmacy Degree. https://www.acpe-accredit.org/pdf/Standards2016FINAL.pdf (Accessed April 2018)
3. Knoer SJ, Eck AR, Lucas AJ.A review of American pharmacy: education, training, technology, and practice. *J Pharm Health Care Sci.* 2016 Nov 9;2:32. eCollection 2016.

PL-14: DESIGN AND ACTIVITY MECHANISM DESCRIPTION OF ANTICANCER ACTIVE BENZAZOLES AGAINST DNA TOPOISOMERASE-II BY USING MOLECULAR MODELING TECHNIQUES

[1] Aki-Yalcin, E., [2] Yilmaz, S., [1] Bolelli, K., [1] Ozturk, O., [1] Ertan-Bolelli, T., [3] Taskin-Tok, T., [1] Yalcin, I.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

[2]Trakya University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Edirne, Turkey

[3]Gaziantep University, Faculty of Science, Department of Chemistry, Gaziantep, Turkey

INTRODUCTION:

Most effective therapeutically active drugs have been discovered and put into market by the use of computer aided drug design studies in the recent years. There has been considerable interest in DNA topoisomerases over the last decade, as they are shown to be one of the major cellular targets in anti-cancer drug development [1]. Formation of protein-concealed DNA strand breaks, resulting in the stabilization by the drug of an intermediary complex of the Topoisomerase-II reaction is related to the antitumor activity. In the recent years our research team have been working with heterocyclic compounds, benzazoles and their DNA Topoisomerase-II inhibitory activities. Some of them were found to be more active than the reference drug, Etoposide [2-6].

MATERIALS AND METHODS:

CoMFA/CoMSIA analysis were performed, pharmacophore and molecular docking studies were carried out to predict the binding properties between Topoisomerase-II enzyme and the synthesized benzazole compounds using the Sybyl 6.6 Software and Discovery Studio 3.5 [7].

RESULTS:

The results observed by CoMFA/CoMSIA studies were revealed that the electrostatic and the hydrophobic molecular descriptors are more significant than the molecular steric fields of the tested compounds. The observed pharmacophore hypothesis and docking performed were shown that hydrogen bond acceptor groups are important for binding to the receptor side.

CONCLUSIONS:

Some of the synthesized benzazole derivatives are found appreciable for the treatment of different multidrug-resistant cancer cells with cross resistance against ‘‘classical’’ Topo II-targeting drugs.

REFERENCES:

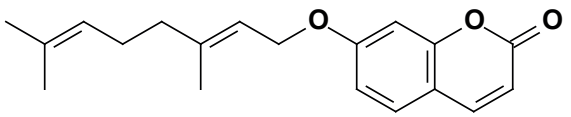
1. Cho KH, Pezzuto JM, Bolton JL, Steele VE, Kelloff GJ, Lee SK (2000). Eur. J. Cancer, 36:2146-2156.
2. Pinar A, Yurdakul P, Yildiz I, Temiz-Arpaci O, Acan NL, Aki-Sener E, Yalcin I (2004). Biochem. Biophys. Res. Comm., 317:670-674.
3. Kaplan-Ozen C, Tekiner-Gulbas B, Foto E, Yildiz I, Diril N, Aki-Yalcin E, Yalcin I (2013). Med. Chem. Res., 22:5798-5808.
4. Zilifdar F, Alper-Hayta S, Yilmaz S, Kaplan-Ozen C, Foto E, Aydogan Z, Yildiz I, Aki E, Yalcin I, Diril N (2014). Med. Chem. Res., 23:480-486.
5. Aki-Yalcin E, Ertan-Bolelli T, Taskin-Tok T, Ozturk O, Ataei S, Ozen C, Yildiz I, Yalcin I (2014). SAR QSAR Environ. Res., 25:637-649.
6. Zilifdar F, Foto E, Ertan-Bolelli T, Aki-Yalcin E, Yalcin I, Diril N (2018). Arch. Pharm., 351:1-8.
7. Dassault Systèmes BIOVIA, Discovery Studio 3.5, San Diego, CA, USA, (2012).

PL-15: AURAPTENE: A SURVEY OF ITS PHYTOCHEMICAL AND PHARMACOLOGICAL PROFILE

Epifano F.

University “G. d’Annunzio” of Chieti-Pescara, Department of Pharmacy, Chieti Scalo (CH), Italy

Auraptene (7-geranyloxycoumarin) **1** is the most abundant prenyloxycoumarin occurring in nature (1).



1

This secondary metabolite has been isolated for the first time at the beginning of 30’s by Komatsu and cowokers from fruit peels of *Citrus aurantium* L. (bitter orange) and then shown to be a common coumarin-based phytochemical of plants belonging to the families of Rutaceae, Apiaceae, Compositae, Euphorbiaceae, and Polygalaceae, including several medicinal and edible herbs (2,3). Among such plant species, the genus *Citrus* still represent the most abundant source of auraptene. This coumarin has been also recently revealed as a component of bee products like propolis (4). Furthermore this oxyprenylated coumarin can be obtained in very high yield and purity by an easy to handle one-step synthetic scheme from commercially available umbelliferone. During the last two decades auraptene was found to possess a great therapeutic potential and several beneficial effects for human welfare both *in vitro* and *in vivo* as dietary feeding cancer chemopreventive, neuroprotective, immunomodulatory, anti-bacterial, anti-protozoal, anti-inflammatory, anti-platelet aggregation, spasmolytic and anti-oxidant agent. The mechanism of action underlying the observed effects comprise triggering important biological targets like metalloproteinases, PPARs, monoaminooxidase, GLUT4, FXR, hOAT1 and hOAT3, and several others. The aim of this lecture will be the provided an updated and detailed survey of the phytochemical and pharmacological properties of the title natural products.

REFERENCES:

1. Genovese S, Epifano F (2011). Current Drug Targets, 12, 381-386.
2. Taddeo VA, Epifano F**,** Fiorito S, Genovese S (2016). Journal of Pharmaceutical and Biomedical Analysis*,* 129, 219-223.
3. Taddeo VA, Genovese S, de Medina P, Palmisano R, Epifano F**,** Fiorito S (2017). Journal of Pharmaceutical and Biomedical Analysis, 134, 319-324.

PL-16: OPPORTUNITY AND CHALLENGES OF NASAL POWDERS: DRUG FORMULATION AND DELIVERY

[1,2] Tiozzo Fasiolo, L., [2] Bortolotti, F., [1] Sonvico, F., [1,3] Balducci, A.G., [4] Russo, P., [2] Colombo, G.

[1] University of Parma, Department of Food and Drug Sciences, Parma, Italy

[2] University of Ferrara, Department of Life Sciences and Biotechnology, Ferrara, Italy

[3] University of Parma, Biopharmanet TEC, Parma, Italy

[4] University of Salerno, Department of Pharmacy, Fisciano (SA), Italy

Nowadays, the majority of marketed nasal products are liquids, delivered as sprays or drops. However, instability, drug dosage requirements and rapid clearance from the nasal cavity are significant drawbacks. Solid dosage forms, mostly powders, are more stable than liquids. They denote a simpler composition in excipients, allowing for the administration of larger drug doses. Powders also facilitate the formulation of poorly water-soluble compounds (Tiozzo Fasiolo et al., 2018). They enhance drug diffusion and absorption across the mucosa, thus improving drug bioavailability at the site of action.

This paper focuses on the opportunities and challenges of developing powders for nasal drug delivery. Thalidomide, desmopressin and ribavirin are examples of molecules of interest respectively for

local and systemic action as well as for nose-to-brain delivery. Nasal powder formulations of thalidomide were designed for use in hereditary hemorrhagic telangiectasia as a local anti-epistaxis therapy after discontinuing oral treatment (Colombo et al., 2016).

The antidiuretic peptide desmopressin, formulated as chimera agglomerates to improve drug bioavailability and provide a flexible drug product, significantly reduced urine production in rats after nasal administration (Balducci et al., 2013).

Finally, ribavirin, an antiviral drug potentially useful to treat viral infections both in humans and animals, was formulated in the form of agglomerates comprising micronized drug and spray-dried microparticles containing excipients with potential absorption enhancing properties (mannitol, chitosan, and α-cyclodextrin). *In vivo* nasal administration to rats of the agglomerates containing α-cyclodextrin led to higher drug accumulation in all the brain compartments analyzed as compared with the micronized administered as such without excipient microparticles (Colombo et al., 2011; Giuliani et al., 2017).

REFERENCES

1. Tiozzo Fasiolo et al. (2018). Eur. J. Pharm. Sci., 113:2-17.
2. Colombo G. et al. (2016). Int. J. Pharm., 514(1):229-237.
3. Balducci A.G. et al. (2013). Int. J. Pharm., 440(2):154-160
4. Colombo G. et al. (2011). Antiviral Res., 92(3):408-414.
5. Giuliani A. et al. (2018). Drug Deliv., 25(1):376-387

PL-17: HYBRID NANO(BIO)MATERIALS: NEW ANALYTICAL TOOLS FOR THE DEVELOPMENT OF (BIO)SENSORS

Rivas, G.

INFIQC (CONICET)-Departamento de Fisicoquímica. Facultad de Ciencias Químicas. Universidad Nacional de Córdoba. Ciudad Universitaria. 5000 Córdoba. Argentina

This presentation will describe new avenues for the design of (bio)analytical platforms based on the use of carbon nanomaterials. Special emphasis will be given to the rational selection of the functionalizing agent to obtain nanostructures with particular recognition properties, either DNA-intercalator; enzyme-substrate and avidin-biotin, among others. The importance of the strategy used to functionalize the carbon nanomaterials will be critically discussed with different examples: a)multi-walled carbon nanotubes non-covalently modified with proteins, DNA and peptides; b) single-walled carbon nanotubes covalently modified with aminoacids and peptides; and c)graphene oxide integrated in supramolecular architectures by self-assembling of polymers/biomolecules. The advantages of electrochemical and plasmonic (bio) sensors obtained by modification of glassy carbon and gold surfaces with the resulting functionalized carbon nanomaterials will be demonstrated in connection with the quantification of different (bio) markers of clinical and environmental relevance like neurotransmitters, DNA, glucose, galectine 3, purines, phenolic compounds and heavy metals.

In summary, the judicious functionalization of carbon nanomaterials, the robust immobilization of the resulting modified nanohybrid materials at the transducer surfaces, and their efficient incorporation in supramolecular architectures, make possible the development of highly sensitive and selective bioanalytical platforms for the quantification of (bio) markers.

ACKNOWLEDGEMENTS:

The authors acknowledge to CONICET, SECyT-UNC, ANPCyT and MINCyT-Córdoba for the financial support.

PL-18: WHAT IS HAPPENING AT THE NANOENVIRONMENT OF CARBON NANOSTRUCTURES? DEMOLITION OF TABOOS!

Degim, IT., Degim, Z., Camlik,G.

Biruni University, Department of Pharmaceutical Technology, Zeytinburnu [3]4010, Istanbul, Turkey

Nanotechnology provides new insights and a variety of tools for developing new and futuristic drug delivery systems[1]. These types of systems can enhance solubility or stability of active molecules and modified surfaces can provide a better delivery, precise targeting etc. Many attempts have been trying to develop these nanosystems considering their surfaces, physical properties and some size related characteristics. Most of them have been only focusing on the drug delivery systems but the characteristics of water in the formulation or at the site of action can actually be altered with these nanomaterials when they are formulated together. For instance, if nanotubes are formulated in water; they can have water molecules on the surfaces or water molecules can go inside of the nanotubes. If any of these happened, the thermodynamic and properties of water molecules can be totally changed. These alterations affect the energy state, dissolving or solvation capability of water molecules at the nanoenvironment. All these have not been considered and all interpretations have been made in wrong direction so far. Positive or gained properties have been always attributed only to the nanodelivery system. Recent reports from other scientific fields[2] have mentioned that water molecules

can travel to the inside of the carbon nanotubes and in this condition, water molecules squeezed in the tubular structures in a very small scale, it forms into an entirely new type of molecule, a new state of water occurs and these molecular arrangements actually change the properties of water molecules in the formulation unexpectedly.

This talk aims to announce and highlight how the alterations of water or solvent molecule properties by these nanosystems can be possible when they formulated together. Some new interpretations with supporting evidences by focusing on the results and properties of water molecules at nanoenvironment will be provided and the key structure–property relationships, interactions and their effects on drug release, delivery and their penetrations will be discussed.

REFERENCES:

1. Degim et al. Carbon nanotubes for transdermal drug delivery, J Microencapsul. 27(8): 669-681 (2010).
2. Youn, SK et al. (2014).,In: L. Mercury et al. (eds.), Transport and Reactivity of Solutions in Confined Hydrosystems, NATO Science for Peace and Security Series C: Environmental Security, Springer, Science + Business Media, Dordrecht. Netherlands, pp 19-26.

PL-19: ANTIVIRULANCE STRATEGIES AGAINST MEDICALLY IMPORTANT CANDIDA SPP.

Kosalec, I.

University of Zagreb, Faculty of Pharmacy and Biochemistry, Schrottova 39, HR-10000 Zagreb, Croatia; e-mail: ikosalec@pharma.hr

Since the well-known physiological way of disruption of life cycle of medically important fungi by active substances currently registered as medicines and consequently the emerging of resistance to such medicines, the new paradigmatic shift at microbial target started. Knowing the complex life of *Candida* spp. and interaction between the host's attributes are possible way to find a new target for medicines. Since we know the atributes of fungal virulence and steps during interaction between the host's factors, we could modulate those complex systems. The yeast such such as *Candida* spp. are as the most potent target for such a research. New strategies towards eradication or prevention of fungal infection include inhibition of adherence to biological and non-biological surafces, such as catheters or implants by modulation of cell-curface hydrophobicity (CSH) and modulation of surface-based receptors. Small molecular weight inhibitory molecules against yeast germination and with inhibitory activity against hydrolitic enzymes such as proteases and phospholipases are also in antifungal medicines pipeline. New strategies include also new targets in yeast cells. Fungicidal activity of ROS-producing molecules or nanoparticles, modulation of not well studied steps in survival and fitness of yeast cells in host (modulation of calcineurin or Hsp90 or sphinglipid sythesis pathways); application of specific monoclonal antibodies or radioimmunotherapy; potentisation of known antifungals with molecules not indicated for fungals infection (statins, NSAIDs) are examples of novel targets. The use of synthetic peptides (antimicrobial peptides, AMP) or those derived from human source (defensins, histatins) against fungal infection are in late clinical phases. Many medicines express also antifungal activity against medically important fungi and such medicines could be repurposed (verapamil, rifampin, rapamycin etc.). Besides the improvents of current antifungals by structural modification brand new paradigmatic research area emerge within the antifungal pipeline. During the presentation examples of methodological approach in vitro and examples of novel molecules together with a clinical outcome will be given.

REFERENCES:

1. J. R. Perfect (2017) Nature Reviews Drug Discovery, 16: 603-616
2. I. Zorić, I. Kosalec et al. (2017) BMC Complement Altern. Med. 17

PL-20: SIMPLE, RELIABLE AND VERSATILE ELECTROANALYTICAL BIOPLATFORMS FOR EARLY DIAGNOSIS OF CANCER AT DIFFERENT MOLECULAR LEVELS

Pingarrón, J.M., Campuzano, S., Torrente-Rodríguez, R.M., Ruiz-Valdepeñas Montiel, V., Vargas, E., Povedano, E., Pedrero, M.

Unıversıdad Complutense de Madrid, Facultad de Ciencias Químicas, Madrid, 28040, Spain

INTRODUCTION:

Giving the increasing cancer incidence and prevalence in the last years, the development of efficient, simple, quantitative and disposable devices with short response times, low-cost, and suitable to perform decentralized and reliable determination of early diagnosis biomarkers could help significantly reducing cancer mortality. Within this context, this talk will present different strategies based on the use of novel electrochemical bio-platforms for the sensitive, selective and rapid biosensing, individually or multiplexed, of biomarkers of different molecular levels associated with early cancer diagnosis

MATERIALS AND METHODS:

The developed methodologies are based on the appropriate use and coupling of novel bioreceptors, functionalized magnetic microcarriers, attractive bioassays formats and amperometric transduction at disposable transducers, both unmodified and

nanostructured.

RESULTS:

In particular, the most relevant characteristics of new electroanalytical platforms for the determination of human protein biomarkers of well-accepted and emerging clinical relevance [1], autoantibodies against tumor associated antigens (TAAs) [2], specific mutations [3], miRNAs [4], and altered DNA methylation patterns [5] will be discussed. All the developed methodologies demonstrated excellent features and reliable determination of the target analytes at clinically relevant levels in highly complex biological samples: cancer cells, human tissues (fresh and paraffin) and liquid biopsies.

CONCLUSIONS:

These platforms for individual or multiple analysis of cancer biomarkers provide results in line with those of conventional methodologies but in less time and with simpler protocols and lower cost. These features made them particularly attractive for their implementation in easy-to-use and affordable devices to perform routine determinations in both clinical and basic research settings to improve cancer diagnosis. In addition, the methodologies developed can easily be extended to the determination of other biomarkers of clinical relevance.

REFERENCES:

1. Torrente-Rodríguez et al. (2016). Biosens. Bioelectron., 77:543-548.
2. Garranzo-Asensio et al. (2016). Anal. Chem., 88:12339-12345.
3. Esteban-Fernández de Ávila et al. (2015). Anal Chem., 8:2290-2298.
4. Zouari et al. (2017) Biosens. Bioelectron,. 91:40–45.
5. Povedano et al. (2018) Sci. Rep. 8:6418 | DOI:10.1038/s41598-018-24902-1.

PL-21: GLYCOPHARMACY: A NEW STAR ON THE HORIZON

Dumić, J.

University of Zagreb Faculty of Pharmacy and Biochemistry,

Department of Biochemistry and Molecular Biology, Zagreb, Croatia

Glycosylation is a complex and structurally most diverse posttranslational modification that affects >80% of all human cell membrane and secreted proteins, as well as many intracellular proteins. Due to their huge structural diversity, glycans are ideal molecular media for storing biological information. Their highly specific interaction with physiological receptors enable variety of biological processes (cell proliferation, differentiation, motility, adhesion, apoptosis, cell-cell and cell-matrix interactions etc.), thus being involved in numerous physiological and pathophysiological processes, from fertilization through embryogenesis and development, to immunity, aging, cancer and metastasis spreading. Consequently, glycan-protein interactions have become potential targets for therapeutic intervention, while carbohydrate-based drugs started to attract huge attention of pharmaceutical industry. Recent developments in the field of glycan analysis and synthesis enabled, not only development of new therapeutic compounds based on carbohydrates, but also understanding of glycosylation changes related to different diseases. Some of them seem to be highly specific and may serve as valuable diagnostic or prognostic biomarkers. Furthermore, changes in glycosylation of transportation proteins in serum may affect bioavailability of drugs while correct glycosylation of therapeutic proteins (monoclonal antibodies, hormones, growth factors etc.) is of utmost importance for their biological and therapeutic activity. This is why glycopharmacy arises as a new star on the horizon not only in the pharmacy field but also in personalised medicine, in general. The recent achievements, as well as further challenges in the field will be overviewed in the presentation.

PL-22: MOLECULARLY IMPRINTED POLYMERS FOR A TARGET COMPOUND AND ITS HALOGENATED DERIVATIVES AND THEIR IMPRINTING EFFECTS

Haginaka, J.

Mukogawa Women's University, School of Pharmacy and Pharmaceutical Sciences, Nishinomiya, Japan

INTRODUCTION:

Molecularly imprinted polymers (MIPs), which selectively recognize a target compound and its structurally related analog(s), have been shown to be useful as selective sorbents. Suspension polymerization, seed polymerization (multi-step swelling and polymerization) and precipitation polymerization give microspherical beads. Among those, the latter two methods could yield monodisperse MIPs. In this study, we prepared monodisperse MIPs for warfarin (WF) and its halogenated derivatives [4′-chlorowarfarin (coumachlor, cWF) and 4′-bromowarfarin (bWF)] by multi-step swelling and polymerization and evaluated their imprinting effects by LC. Furthermore, MIP_{cWF} was used for the assay of WF as a pretreatment column by column-switching technique.

MATERIALS AND METHODS:

MIPs for WF, cWF and bWF (MIP_{WF}, MIP_{cWF} and MIP_{bWF}, respectively) were prepared using 4-vinylpyridine (4-VPY) and ethylene glycol dimethacrylate (EDMA) as a functional monomer and crosslinker, respectively.

Similarly, non-imprinted polymers (NIPs) were prepared. The retenton factor (k) and imprinting factor (IF = k_{MIP}/k_{NIP}) of WF, cWF and bWF on the obtained MIPs were evaluated in reversed-phase LC.

RESULTS:

In addition to shape recognition, hydrogen bonding, ionic and hydrophobic interactions work for the retenition and recogntion of WF, cWF and bWF on the MIPs. The IFs for WF, cWF and bWF were in the order of $MIP_{WF} < MIP_{cWF} < MIP_{bWF}$. It is interesting that WF is more recognized on MIP_{cWF} and MIP_{bWF} than MIP_{WF}, i.e. IF of WF is larger on MIP_{cWF} and MIP_{bWF} than MIP_{WF}. This suggests that in the imprinting sites, microenvironmental changes of 4-VPY-*co*-EDMA MIP_{cWF} and MIP_{bWF} might occur. Furthermore, MIP_{cWF} was successfully used for the assay of WF in rodenticides and biological fluids as a pretreatment column by column-switching technique.

CONCLUSIONS:

The above results indicate that the use of cWF or bWF as a template molecule instead of WF could be useful for getting a higher IF for WF and for avoiding the leakage problem in the assay of WF in LC.

REFERENCES:

1. Nakamura Y, Masumoto S, Kubo A, Matsunaga H, Haginaka J (2017). J. Chromatogr. A, 1516:71-78.

PL-23: SEARCH FOR BIOACTIVE MOLECULES FROM OKINAWAN CORAL REEF ORGANISMS AND METABOLITE DIVERISTY OF SOME ORGANISMS

Tanaka, J.

University of the Ryukyus, Department of Chemistry, Biology and Marine Science, Okinawa 90[3]-021[3], Japan

INTRODUCTION:

Marine organisms in Okinawa, southwest part of Japan, have been the subjects for bioprospective studies from late 1970s. As results, a large number of unique molecules both in structure and bioactivity have been reported. Although there are many chances to encounter known metabolites in a classical natural products study, thanks to the species diversity, there still exists a chance to discover newer bioactive molecules. In this talk, our recent works together with biodiversity aspects will be presented.

MATERIALS AND METHODS:

Coral reef organisms were collected by hand using scuba or rebreather diving. The material were mostly screened by collaborators and the hit molecules were characterized with spectroscopic data, chemical conversions, and calculation study.

RESULTS:

In addition to known metabolites, aromatic sulfates from the crinoid *Alloeocomatella polycladia* have been identified as enzyme inhibitors against HCV NS3 helicase.[1] Spongian diterpenes from the sponge *Hyattella* aff. *intestinalis*,[2] a new cyclic imine named kabirimine from a cultured dinoflagellate, and metachromin B from the sponge *Dactylospongia metachromia*[3] were found to show antiviral activity against AdV, RSV, and HBV, respectively. In addition, severlal natural products, a macrolide named acidiscalide[4] and a few terpenoids, have been reported.

On our interest on the relation of metabolite diversity with genetic variation of marine organisms, diterpene constituents of the soft corals of the genus *Sarcophyton* were reported previously. [5] We examined the chemical and genetic variations of the nudibranch *Phyllidiella pustulosa*, a common species in Okinawan coral reef.

CONCLUSIONS:

We still believe that macro- and micro-organisms in coral reefs provide newer and bioactive molecules.

REFERENCES:

1. Hermawan et al., (2017). Marine Drugs, 15, 117.
2. Ahmadi et al., (2017). Chem. Pharm. Bull. 65. 874-877.
3. Yamashita et al., (2017). Antiviral Res. 145, 136-145.
4. Agena et al., (2016). Nat. Prod. Commun. 11, 219-221.
5. Aratake et al., (2012). PloS ONE, e30410.

PL-24: ANTI-INFLAMMATORY ACTIVITY OF VARIOUS PRENYLATED PHENOLIC COMPOUNDS

[1] Šmejkal,K. [1] Brezáni, V. [2] Hošek, J.

1 University of Veterinary and Pharmaceutical Sciences Brno, Faculty of Pharmacy, Department of Natural Drugs, Palackého 1946/1, 61[2]4[2], Czech Republic, karel.mejkal@post.cz

[2] University of Veterinary and Pharmaceutical Sciences Brno, Faculty of Pharmacy, Department of Molecular biology and Pharmaceutical Biotechnology, Palackého 1946/1, 61[2]4[2], Czech Republic

INTRODUCTION:

Phenolic compounds can be divided into several categories with the common structural feature of phenolic hydroxyl. Their biological activity is often enhanced by so called prenylation, where the type of the prenyl connection and modification affects the bio-activity. The lecture would shortly summarize the effects of prenylated phenolics in vitro in cellular or biochemical systems on the production and release

of inflammation-related cytokines; their effects on the inhibition of cyclooxygenases and lipoxygenases; the effects on the production of nitric oxide, an antiradical and antioxidant activity, and the effect on the inhibition of the release of enzymes and mediators from neutrophils, mast cells and macrophages. Some selected prenylated flavonoids, 2-arylbenzofurans, and stilbenes as potential antiphlogistic substances will be discussed in detail.

The information about the antiphlogistic potential of prenylated phenolics gives the idea that a big pool of natural prenylated phenols represents a source of inspiration for synthesis, and that prenylated phenols are active principles of various medicinal plants used to combat inflammation (1).

ACKNOWLEDGEMENT:

The financial support of GACR no. 16-07193S project is gratefully acknowledged by K.Š. and J.H.

REFERRENCES:

1. Brezáni V, Šmejkal K, Hošek J, Tomášová V (2018). Current Medicinal Chemistry, 25: 1094-1159.

PL-25: POTENT AND BROAD SPECTRUM MEDICINAL DRUGS AGAINST ALL GENOTYPES OF HEPATITIS C VIRUS (HCV)

[1] Elsebai, MF. , [2] Hakkola, J., [3] Mehiri, M., [4] Diez, J.

[1]Department of Pharmacognosy, Faculty of Pharmacy, Mansoura University, Egypt.

[2]Pharmacology and Toxicology Unit, Institute of Biomedicne, University of Oulu, FIN-90014, Finland.

[3]Nice Institute of Chemistry, University Nice Sophia Antipolis, France.

4Department of Experimental and Health Sciences, Universitat Pompeu Fabra, Barcelona, Spain.

As many as 200 million people worldwide are infected with hepatitis C virus (HCV). About 3–4 million people are infected per year, and ~500,000 people die yearly from hepatitis C-related diseases, (WHO, June 2011). The Egyptian community is suffering from the prevalence of HCV infections 1. Even in the advanced countries hepatitis C is common. HCV is the most common chronic blood-borne infection and it is the most frequent indication for liver transplantation [2]. In the United States, hepatitis C is the most common chronic blood-borne infection (http://www.cdc.gov/hepatitis/HCV/ index.htm).

The infection with HCV is often asymptomatic but chronic infection leads to liver cirrhosis which usually develop into liver failure, liver cancer or life-threatening esophageal and gastric varices. The diseased-liver person usually undergoes subsequent psychological disorders due to the stress of disease which complicates the illness [3]. There is no preventive vaccine available for HCV due to its highly mutable nature evidenced by the presence of more than 50 subtypes of HCV; in addition HCV infects only humans and chimpanzees [4]. Fortunately, Dorner et al [5]and a vaccine is not available. Development of more efficient therapies has been hampered by the lack of a small animal model. Building on the observation that CD81 and occludin (OCLN, were able to complete the entire HCV life cycle in genetically humanized transgenic mice with stably expressing human CD81 and OCLN and blunting the antiviral immunity in these mice infected with HCV.

In the present study, the water extract of the leaves of the wild Egyptian artichoke (WEA) (*Cynara cardunculus* L. var. *sylvestris* (Lam.) Fiori) showed improvement of HCV infection symptoms. Therefore, our study was divided into two main strategies:

1) The clinical investigation of WEA extract on some infected Egyptian patients (approved by the Ethical Committee of Research at the Faculty of Pharmacy, Mansoura University, Egypt, code number 2014/71). The results showed outstanding activity against HCV and its complications such as ascites and jaundice by measuring the PCR, and liver functions such as ALT, AST[6]identify bioactive chemicals in its extract and to tentatively examine the potential inhibitory interactions of WEA with human drug-metabolizing enzymes. The current pilot clinical trial revealed that the water extract of a WEA plant decreased the HCV viral load below the detection level in 12 out of 15 patients. Furthermore, the liver enzymes ALT and AST, as well as the level of bilirubin were normalized. The total WEA extract inhibited CYP2B6 (OH-BUP.

2) The phytochemistry of the WEA extract and its subsequent evaluation of inhibition capacity *in vitro* using cell-culture derived HCV: The chemical investigation of the WEA extract resulted in the identification of six compounds: a new sesquiterpene lactone (**1**), in addition to the known compounds (**2**-**6**). Their structural elucidation was done by extensive spectroscopic tools such as NMR and HR-MS spectroscopy. The absolute configuration was determined by TDDFT ECD calculations and comparison with the experimental CD spectra. The quantitative determination was achieved through UPLC-MS quantitation. Importantly, all compounds inhibited HCV infection; compounds **1** and **2** were the most potent among the six. The EC_{50} were estimated at 1.03 μM, 1.27 μM and 299 μM for compounds **1**, **2** and WEA extract, respectively, by using a luciferase-carrying reporter virus. Time-of-addition experiments revealed that compounds **1** and **2** inhibit HCV virus at a time-point during entry. Furthermore, compounds **1** and **2**, apart from cell-free infection inhibited HCV cell-cell transmission. Finally, the results showed that compounds **1** and **2** inhibited HCV particles from genotypes 1a, 1b, 2b, 3a, 4a, 5a, 6a and 7a indicating that these compounds inhibit HCV cell entry

independently of viral genotype or subtype. Thus, these compounds are promising candidates for the development of new pangenotypic entry inhibitors for the HCV infection[7,8]. All of these results were applied for patenting.

REFERENCES

1. El-Fakharany, E. M., Sanchez, L., Al-Mehdar, H. A. & Redwan, E. M. Effectiveness of human, camel, bovine and sheep lactoferrin on the hepatitis C virus cellular infectivity: comparison study. *Virol. J.* **10,** 1–10 (2013).
2. Haid, S. *et al.* A plant-derived flavonoid inhibits entry of All HCV genotypes into human hepatocytes. *Gastroenterology* **143,** 213–222 (2012).
3. Takebe, Y. *et al.* Antiviral Lectins from Red and Blue-Green Algae Show Potent In Vitro and In Vivo Activity against Hepatitis C Virus. *PLoS One* **8,** e64449 (2013).
4. Houghton, M. The long and winding road leading to the identification of the hepatitis C virus. *Journal of Hepatology* **51,** 939–948 (2009).
5. Dorner, M. *et al.* Completion of the entire hepatitis C virus life cycle in genetically humanized mice. *Nature* **501,** 237–241 (2013).
6. Elsebai, M. F., Abass, K., Hakkola, J., Atawia, A. R. & Farag, M. a. The wild Egyptian artichoke as a promising functional food for the treatment of hepatitis C virus as revealed via UPLC-MS and clinical trials. *Food Funct.* **7,** 3006–3016 (2016).
7. Elsebai, M. F. *et al.* Pan-genotypic hepatitis C virus inhibition by natural products derived from the wild Egyptian artichoke. *J. Virol.* **90,** 1918–1930 (2016).
8. Elsebai, M. F., Mocan, A. & Atanasov, A. Cynaropicrin: a comprehensive research review and therapeutic potential as an anti- hepatitis C virus agent. *Front. Pharmacol.* **7,** Article 472 (2016).

PL-26: TOXIC EFFECTS OF MYCOTOXINS IN HUMANS

Peraica M.

Institute for Medical Research and Occupational Health, Zagreb, Croatia

Mycotoxins are products of moulds that contaminate all kinds of food and feed. Humans are continuously exposed to mycotoxins mostly by ingestion, but other ways of exposure (such as respiratory and dermal) are also possible. Foods of plant origin, such as grains and bread, coffee, grapes and vine, beer and spices are contaminated following infection with mycotoxin-producing moulds, while food of animal origin contains mycotoxins if animals are fed with contaminated feed. Mycotoxins may cause intoxications (either acute or chronic) called mycotoxicoses with high variability of target organs. These may be hepatotoxic, nephrotoxic, immunotoxic, neurotoxic, cardiotoxic, haematotoxic and also have carcinogen and teratogen properties. The severity of mycotoxicoses depends on the toxicity of the mycotoxin, extent of exposure and nutritional status of the individual and possible synergistic effect of other chemicals to which an individual is exposed. The toxic effects of mycotoxins are mostly known from veterinary practice. Mycotoxicoses, which can occur both in industrialized and developing countries, appear when environmental, social and economic conditions are combined with meteorological conditions (humidity and temperature) that favour the growth of moulds.

Mycotoxins have highly variable chemical structures, but being organic compounds of low molecular mass, they do not cause allergies. Out of about 400 mycotoxins, only a few have known toxic effects in experimental animals, and even fewer possess effects known to be toxic in humans. Most mycotoxicoses were first recognized in domestic animals and it is difficult to diagnose them in humans. In humans, mycotoxicosis should be considered in case when a disease appears in several persons, with no obvious connection to a known etiological agent, such as microorganisms. Unfortunately, medical doctors are not trained well to diagnose them, and mycotoxicoses very often remain unrecognized.

There are several international organizations and agencies (such as World Health Organization, International Agency for Research on Cancer and European Food Safety Agency) that deliver scientific opinions on various chemicals in food. The scientific opinion is based on results published in scientific literature on the effects of a toxin in laboratory animals. Researchers have realised that, in the field of mycotoxin toxicology, a particular problem is co-contamination of food with several mycotoxins with antagonistic, additive and synergistic toxic effects. Unfortunately, studies on the combined exposure to two or more mycotoxins are rare and inconclusive.

PL-27: NEW TRENDS IN THE RESEARCH OF BIOACTIVE PLANT SAPONINS

Lacaille-Dubois, MA.

Université de Bourgogne Franche-Comté, UFR des Sciences de Santé, Laboratoire de Pharmacognosie, PEPITE EA 4²67, BP 87900, ²1079 Dijon cedex, France

E-mail address: m-a.lacaille-dubois@u-bourgogne.fr

Saponins are a vast group of triterpene or steroid glycosides, widely distributed in the terrestrial plants and in some marine organisms, including a high number of biologically active compounds. They are

constituents of many plant drugs and folk medicines with veinotonic, anti-edematous, anti-phlogistic, expectorant, adaptogenic, wound healing activities amongst others and are rarely toxic when taken orally... Their amphiphilic character and biological properties have led to increasing applications in the food, cosmetic and pharmaceutical sectors. For more than twenty years, our research group has been deeply involved in the discovery of new bioactive plant saponins, understanding their mechanism of action, and structure/activity relationships. Thanks to worldwide collaborations, mainly in Asia, South America and Africa, we have selected plants according to chemotaxonomic and ethnopharmacological criteria. We used conventional and more recently innovative procedures in accordance with green chemistry leading to the extraction and isolation of these highly complex glycosides possessing up to nine sugar units. Their structural elucidation is performed by sophisticated 2D NMR and mass spectroscopic techniques. The pharmacological potential is evaluated by using bioassays mainly in the field of cancerology, immunology and microbiology. Thus, we isolated and characterized a large number of new bioactive saponins from the Polygalaceae, Caryophyllaceae, Mimosaceae, Pittosporaceae, Fabaceae, Apiaceae, Sapindaceae, Dioscoreaceae, and Asparagaceae families, to mention just a few. Some of them were found to be cytotoxic on cancer cells, immunomodulators, apoptosis inducers on Jurkat cells, inhibitors of the production of Il-1β, and antifungal on *Candida* yeast species.

This lecture will broadly cover our most relevant findings from this multidisciplinary approach, and some future challenges, with latest developments of the scientific literature on saponins as potential adjuvants when they are co-administered with anticancer, antimicrobial, anti-inflammatory drugs, and with antigens in vaccines. This may provide an exciting road for further developments in the treatment of some cancers, parasitic and inflammatory diseases and in the rational design of vaccines against infectious diseases. We will highlight the potential benefit of the most promising immunoadjuvant saponin QS-21 from *Quillaja saponaria* in several vaccine clinical trials with a favorable ratio efficacy/toxicity.

PL-28: POTENTIAL SECONDARY METABOLITES FROM INDONESIAN FUNGI AND ALGAE FOR PHARMACEUTICALS AND COSMETICS

Singgih Wibowo, M.

School of Pharmacy, Bandung Institute of Technology (ITB), Indonesia

Fungi has tremendous benefits to Pharmacy and Cosmetic area. In Indonesia, some of indigenous fungal isolates had been explored to be developed as active ingredients or some excipients for Pharmaceuticals and Cosmetic preparations. Their role and activities in pharmacy can be ranged from active ingredient for lowering cholesterol level such as **lovastatin** or **monacolins** from *Aspergillus terreus* and *Monascus purpureus* , to as food colorants for meats and possibly as cosmetic colorants in lipsticks and rouge products.

Many scientific researches in Indonesia have been focused on development of secondary metabolites of Indonesian fungi, such as *Monascus purpureus, Neurospora intermedia*, and *Aspergillus terreus*. Besides, there are some microalgae have been explored to be utilised for their secondary metabolites for some potential ingredients, such as anti-diabetic polysaccharides from red microalgae *Porphyridum* sp., **DHA** from *Thraustochytrium* sp. and **phycocyanin** from *Spirulina platensis.*

Secondary metabolites from *Monascus spp*, which also developed as natural pigments, have been investigated for its toxicity aspects to guarantee their uses in cosmetics. New **azaphilone** derivates of *Monascus* pigments are further modified to be less toxic.

KEYWORDS :

Secondary metabolites, Fungi, Microalgae

REFERENCES :

1. Marlia Singgih, Vienna Saraswaty, Diah Ratnaningrum, Sri Priatni, Sophi Damayanti, 2014, “The Influence of Temperature and Ethanol Concentration in Monacolin K Extraction from Monascus Fermented Rice””, Procedia Chemistry 9 (2014) , 242 – 247.
2. Sri Priatni, Sophi Damayanti, Vienna Saraswaty, Diah Ratnaningrum, Marlia Singgih, 2014, “The Utilization of Solid Substrates on Monascus Fermentation for Anticholesterol Agent Production. Procedia Chemistry 9 (2014) , 34 – 39.
3. Marlia Singgih, Seno Aulia Ardiansyah, Sophi Damayanti and Sri Priatni, Production of Carotenoid Pigment From *Nuerospora intermedia* N-1: The Influence of Mg2+ , Fe2+ and Cu2+ Ion Cofactor, Oral Presentation and full article in Proceeding of International Conference on Beneficial Microbes ICOBM 2014, 27-29th May 2014, Penang, Malaysia
4. Marlia Singgih, Wendi Andriatna, Sophi Damayanti and Sri Priatni, Carotenogenesis Study of *Neurospora intermedia* N-1 in Liquid Substrate Fermentation, Journal of Chemical and Pharmaceutical Research, 2015, 7(5):842-847.
5. Anna Yuliana, Marlia Singgih Wibowo, Elin Julianti, Solubility and Toxicity Level of

Monascus Pigments, Chiang Mai Journal of Science, Published by Faculty of Science Chiang Mai University, Chiang Mai 50200, Thailand. Submitted with manuscript number: CMJS.07.12.16- 7581, 9 Desember 2016

6. Anna Yuliana, Marlia Singgih, Elin Julianti, Philippe J. Blanc, Derivates of Azaphilone Monascus pigments, Biocatalysis and Agricultural Biotechnology, vol.9, 2017. P.183-194.Available online 28 Desember 2016. Published by Elsevier, Contents lists available at Science Direct. DOI:http://dx.doi.org/10.1016/j.bcab.2016.12.014
7. Anna Yuliana, Marlia Singgih Wibowo, Elin Julianti, Toxicity Level of *Monascus* Pigments Using ECOSAR Program, The 3rd Natural Pigments Conference for South-East Asia (NP-SEA) 2016 , 22 Agustus 2016, Ma Chung University, Jl. Villa Puncak Tidar N-01, Malang 65151, East Java, Indonesia. Oral Presentation and Extended abstract.
8. Marlia Singgih dan Elin Julianti, Role of *Monascus* and *Neurospora* in Pharmacy : Their Metabolites as Active Ingredients and Excipients, Invited Speaker on ICMNS 2016, Bandung,2-3 November, 2016
9. Marlia Singgih, Elin Julianti, Anna Yuliana, The Effect of Different Isolates on Monakolin K Production of Monascus purpureus In Solid Culture, PERMI International Seminar, Palembang, Indonesia, 14-15 November 2017
10. Marlia Singgih and Elin Julianti, Food Colorants from Microorganisms, Chapter in book : Beneficial Microorganism in Food and Nutraceuticals, (Min-Tze Liong, Editor, Alexander Steinbuchel, Series Editor), ISBN. 978-3-319-23176-1, Springer Intl. Publishing, Switzerland, Dec 2015, p.265-284

PL-29: GUT MICROBIOTA AND PROBIOTICS

Yalınay, M.

Gazi University Faculty of Medicine Department of Medical Microbiology Beşevler Ankara

The gut microbiota (GM) is the whole of commensal, symbiotic, and pathogenic microorganisms living in our intestine. The human GM forms a complex ecological community that influences normal physiology and susceptibility to disease through its collective metabolic and immunological activities and host interactions. The GM–host interactions contribute to the maturation of the host immune system, modulating its systemic response. It is well documented that GM can interact with non-enteral cells such as immune cells, dendritic cells, and hepatocytes, producing molecules such as short-chain fatty acids, indole derivatives, polyamines, and secondary bile acid.

A wide variety of commensal microorganisms colonize our body surfaces and gut lumen. For example, there are more than 100 trillion commensal microbes classified into at least 1000 different species in our gastrointestinal tract. Nevertheless, our understanding of the diversity of the gut microbiota was largely limited, and it showed that the gut microbiota is mainly composed of four phyla, namely, Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria. This diversity is very important for health and related conditions. But when one of these bacterial colonies is out of balance, it can lead to dysbiosis.

Moreover, the gut microbiota contains 600,000 genes that called as microbiome, and it is approximately 25 times more than the number of genes in our own genome, highlighting the existence of a highly complex microbiota ecosystem with the potential for profound effects on metabolism and immune function. Intestinal immune, nerve, and endocrine cells are tightly interlinked and form a highly complex gut ecosystem, along with the gut microbiota, through host microbial crosstalk, which contributes to homeostatic balance in the host. Dysbiosis typically occurs when the bacteria in your gastrointestinal (GI) tract which includes your stomach and intestines become unbalanced. Dysbiosis is a term for a microbial imbalance or maladaptation on or inside the body, such as an impaired microbiota. For example, a part of the human microbiota, such as the skin flora, gut flora, or vaginal flora, can become deranged, with normally dominating species underrepresented and normally outcompeted or contained species increasing to fill the void. Dysbiosis is most commonly reported as a condition in the GI tract.

The connection between the microbial world of our gut and other important aspects of health, including immune functioning, chronic gastrointestinal dysfunction, metabolism, and obesity has a substantial interest for health and disease outcomes. Gut dysbiosis, has been associated with several clinically relevant conditions. These conditions include obesity, cardiovascular diseases, liver diseases, kidney diseases, type 1 and type 2 diabetes, rheumatoid arthritis, cancer, and allergic diseases. Moreover, several neurological disorders have been associated with gut dysbiosis.

Gut microbiota metabolic end products are low weight molecular molecules such as short-chain fatty .The receptors for some of these molecules are expressed on immune cells, and modulate the differentiation of T effector and regulatory cells: this is the reason why dysbiosis is correlated with several autoimmune, metabolic, and neurodegenerative diseases. An expanding branch of this research of particular interest to mental health professionals is providing evidence that supports a strong link between the microbial state

of our gut and our emotional functioning, particularly in relation to stress, anxiety and depression. Furthermore, the microbial functions of our gut may also have significant influence on more profound disorders, such as autism. Biologically classified as the enteric nervous system, consisting of nearly 100 million neuronal connections, and the ability to function independently, it is often referred to as the second brain. An abnormal microbiota associated with a disrupted gut barrier and the activation of the mucosal immune system leads to the release of inflammatory mediators and other neuroactive molecules into the systemic circulation from where they reach the brain and result in changes in cognition and behavior. Alternately, central stimuli, such as stress, can disrupt mucosal immunity, the gut microbiota and gut barrier function and lead to gut dysfunction. One example of the microbiota–gut–brain axis is in the production and use of serotonin, a neurotransmitter whose imbalance is strongly correlated with depression. Although serotonin is commonly associated with location in the central nervous system, it is found not only in the brain but is also created in the gut. Strikingly, about 95 percent of our serotonin is synthesized by bacteria in the gut.

A discussion about the impact of our gut health and related diseases due to dysbiosis of gut microbiota cannot occur without addressing two very important players: probiotics and prebiotics. Generally, probiotics are known as “friendly bacteria” or “good bacteria.” Probiotics are defined by the World Health Organization and the Food and Agriculture Organization of the United Nations as “live microorganisms, which, when administered in adequate amounts, confer a health benefit on the host”. It is interesting to note that the modern word “probiotic” is derived from words meaning “for life” (Greek pro: for and bios: life).

Most probiotics are microorganisms known as lactic acid bacteria (LAB) and are normally consumed in the form of yogurt, fermented milks, or other fermented foods. LAB are known to exert a wide range of effects on the immune system, and are defined as “generally recognized as safe” (GRAS). While the most common microorganisms used as probiotics are from the LAB such as lactobacilli, lactococci, and streptococci, these are not the only good bugs in our gut. Bifidobacterium genera and other bacterial genera, including Enterococcus, Streptococcus, and Escherichia, and the yeast Saccharomyces boulardii, are also used as probiotics. A probiotic has been defined as a live microbial food ingredient that, when ingested in sufficient amounts, exerts beneficial effects on health. In order to consider organisms as probiotics, it has to be demonstrated that it should (a) be nonpathogenic and nontoxigenic, (b) have a proven beneficial effect on health, (c) protect against pathogenic microorganisms, (d) be isolated from the same species as its intended host, (e) be able to survive transit of the upper GI tract, (f) adhere to mucus or the intestinal epithelium, (g) temporarily colonize sites in the GI tract, and (h) remain viable for a long time.

Probiotics may help prevent infections, reduce cholesterol levels, promote vitamin and cytokine synthesis and inhibit cancer progression. The safety and efficacy of a given strain in the context of these properties must be scientifically demonstrated for it to be considered a probiotic. Psychobiotics is an interesting defined probiotics group related to gut brain axis and all the conditions (emotional well-being, stress, depression, neurodevelopmental disorders) up to this connection.

Prebiotics, on the other hand, have been defined as nonabsorbable food ingredients that promote the growth or activity of a limited number of bacterial species for the benefit of human health. Prebiotics are found naturally in many foods that provide fermentable fiber, and can also be isolated from plants. The most commonly used prebiotics are carbohydrate substrates such as fructans and nonfructan prebiotics like resistant starch. Synbiotics is the word used for the combined administration of probiotic bacteria with prebiotics that support their growth to provide definite health benefits by synergistic action.

The human gut microbiota forms a complex ecological community that influences normal physiology and susceptibility to disease through its collective metabolic and immunological activities and host interactions. Current studies suggest that manipulation of the gut microbiota could be a promising approach for the prevention and management of disorders.

Moreover, the evidence showed that attempts to treat acute infectious and post-antibiotic gastroenteritis with some probiotics were significantly effective in a great number of patients, leading many experts to suggest the use of probiotics to address all of the clinical problems associated with dysbiosis. The available data are promising, but presently, further studies are needed before probiotics can be considered a reliable treatment for dysbiosis related clinical conditions. Gut microbiota related health and diseases and probiotics are currently most interesting topics in medicine. Personalized medicine essentially will obtain crucial data by means of metagenomic analysis of gut microbiome.

REFERENCES

1. Yamashiro Y. Gut Microbiota in Health and Disease. Ann Nutr Metab. 2017; 71(3-4):242-246. doi: 10.1159/000481627
2. Principi N, Esposito S. Gut microbiota and central nervous system development. J Infect. 2016 Dec; 73(6):536-546. doi: 10.1016/j.jinf.2016.09.010. Epub 2016 Oct 8.
3. He M, Shi B. Gut microbiota as a potential target of metabolic syndrome: the role of probiotics and prebiotics. Cell Biosci. 2017 Oct 25; 7:54. doi: 10.1186/s13578-017-0183-1. eCollection.
4. Principi N, Cozzali R, Farinelli E, Brusaferro A, Esposito S. Gut dysbiosis and irritable bowel syndrome: The potential role of probiotics. J Infect. 2018 Feb; 76(2):111-120
5. Quigley EMM. The Gut-Brain Axis and the Microbiome: Clues to Pathophysiology and Opportunities for Novel Management Strategies in Irritable Bowel Syndrome (IBS). J Clin Med. 2018 Jan 3; 7(1). pii: E6. doi: 10.3390/jcm7010006.
6. Verdino J. The third tier in treatment: Attending to the growing connection between gut health and emotional well-being. Health Psychol Open. 2017 Aug 10; 4(2):2055102917724335. doi: 10.1177/2055102917724335.
7. Dinan TG and Cryan JF. Regulation of the stress response by the gut microbiota: Implications for psychoneuroendocrinology. Psychoneuroendocrinology 2012, 37: 1369–1378.
8. Dinan TG and Cryan JF. Melancholic microbes: A link between gut microbiota and depression? Neurogastroenterology &Motility 2013, 25: 713–719.
9. Bravo JS, Julio-Pieper M, Forsythe P, et al. Communication between gastrointestinal bacteria and the nervous system. Current Opinion in Pharmacology 2012, 12: 667–672.
10. Mayer EA Gut feelings: The emerging biology of gut–brain communication. Nature Reviews Neuroscience 2011, 12: 453–466.
11. Mayer EA, Padua D and Tillisch K. Altered brain-gut axis in autism: Comorbidity or causative mechanisms? BioEssays 2014, 36: 933–939.
12. Yalınay Çırak Meltem. Functional Dairy Products and Probiotics in Infection Diseases 2010, Development and Manufacture of Yogurt and Other Functional Dairy Products. Chapter 14, Page 391-411, Taylor and Francis Group, LLC, USA, ISBN: 978-1-4200-8207-4,
13. Dinan TG, Stanton C and Cryan JF. Psychobiotics: A novel class of psychotropic. Biological Psychiatry 2013, 74: 720–726.

PL-30: THE SIGNIFICANCE OF XENOBIOTIC/DRUG METABOLIZING ENZYME POLYMORPHISMS IN RESPONSE TO CHEMOTHERAPY AND SURVIVAL IN LUNG CANCER PATIENTS.

Iscan, M.

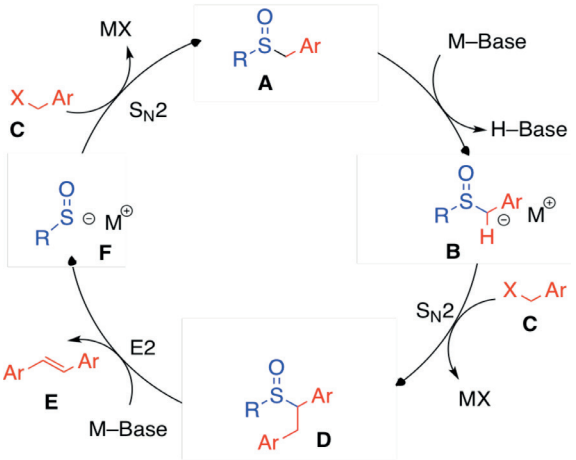
Ankara University, Faculty of Pharmacy, Department of Toxicology, Tandogan, Ankara, Turkey

Lung cancer is an increasing worldwide public health problem particularly in men. The 28 % of deaths arising from cancers are caused by lung cancer. Non-small cell lung cancer (NSCLC) patients represent the majority of lung cancer cases and they are mainly treated with platinum based chemotherapy. However, the poor response and a great interindividual variety in response to this chemotherapy occur in these patients. Thus, the reasons behind the failure and interindividual variety of response to chemotherapy and thus possibly poorer survival in these patients are very important. There is accumulating evidence to support the hypothesis that genetic polymorphisms alter the xenobiotic/drug response and survival. It is well known that majority of lung cancer patients are cigarette smokers. Cigarette smoke has been reported to cause elevated levels of carcinogen DNA-adducts which in turn form aggressive tumors by mutating and thus inactivating tumor suppressor genes (such as TP53) and thereby decrease the survival rates of patients with NSCLC. Carcinogens such as polycyclic aromatic hydrocarbons (PAHs) and nitrosamines in cigarette smoke are activated by cytochrome P450s (CYP)s mainly CYP1A1, CYP1B1 and CYP2E1 and inactivated by Glutathione S-transferases (GST)s such as GSTM1, GSTO1, GSTP1 and GSTT1. These enzymes also play an important role in the metabolism of a number of chemotherapeutic agents and thus involve in the drug efficacy, toxicity and resistance in cancer chemotherapy. CYP and GST genes are found to be polymorphic and the polymorphisms in these genes are associated with changes or loss in enzyme activity. In addition, CYP and GST gene polymorphisms can be associated especially with TP53 (Arg72Pro) gene polymorphism, the mutant genotype of which has reduced apoptotic potential, in the occurrence of more aggressive tumor phenotypes. Thus, CYP, GST and TP53 gene polymorphisms may influence the response to therapy and survival in patients with lung cancer. Herein, recent findings with respect to the role of CYPs (CYP1A1, CYP1B1 and CYP2E1), GSTs (GSTM1, GSTO1, GSTP1 and GSTT1) and TP53 (Arg72Pro) gene polymorphisms in response to mainly platinum-based chemotherapy and survival in patients with NSCLC will be evaluated.

PL-31: 2-AZAALLYL ANIONS AND SULFENATE ANIONS: UNUSUAL AND UNEXPECTED REACTIVITY

Walsch, P

The seminar will outline the Walsh Group's efforts in C–C and C–S bond forming reactions. The Walsh lab has developed a series of Pd and Ni catalyzed deprotonative cross-coupling processes (DCCP) that enable the synthesis of a variety of small molecule building blocks for use in the pharmaceutical industry. The second part of the seminar will outline the introduction of a novel organocatalysts, sulfenate anions, that facilitate the dehydrocoupling of benzylic halides and the formation of alkynes. The dehydrocoupling of benzylic chloromethyl groups to form polymers will also be introduced.



PL-32: DESIGN AND EVALUATION OF A 3D BIOPRINTED IMPLANTABLE DRUG DELIVERY SCAFFOLD FOR APPLICATION IN BONE TISSUE ENGINEERING

Kondiah, P.P.D, Kondiah, P.J., Choonara,Y.E., Marimuthu, T., du Toit, L.C., Kumar, P.,Pilla, V.

Wits Advanced Drug Delivery Platform Research Unit, Department of Pharmacy and Pharmacology, School of Therapeutic Sciences, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, 7 York Road, Parktown, 219³, South Africa

INTRODUCTION:

A 3D bioprinted drug delivery scaffold was synthesised and optimized as a thermo-responsive implantable technology, possessing similar matrix hardness and resilience properties as healthy bone tissue, once incorporated in situ. The 3D bioprinted scaffold was developed using computer aided design (CAD) software, with further optimization of the designed formulations, employing MATLAB® programing and artificial neural networks.

METHODS:

3D bioprinting was undertaken to design an implantable drug delivery scaffold for controlled release of loaded drug. Morphological, artificial neural network studies, in vitro release and optimization studies were undertaken on the implantable scaffold. The prepared formulations were synthesised and polymerically blended to obtain a stimuli-responsive implant. TGA was also undertaken to determine the degree of thermodegradation in the implantable system. Biomaterial testing was employed using a BioTester 5000 Cell scale system, evaluating the tensile strength and viscoelastic nature of the implant.

RESULTS:

The designed scaffold displayed significant bone filling and matrix hardening properties. The 3D bioprinted scaffold demonstrated remarkable properties as a controlled release platform, biodegrading gradually over 20 days and releasing its loaded contents in a sustained manner, allowing contact adhesion between fractured/damaged bone and formation of artificial bone matrix within these sites. SEM analysis confirmed the programmed architecture of the scaffold, with precise pore dimensions for cell biocompatibility.

DISCUSSION:

It was confirmed that the 3D bioprinted drug delivery scaffold has great potential for application in bone fractures, due to its physicochemical and phsicomechanical properties. In vitro release further confirmed gradual biodegradation of the scaffold, with ideal bone matrix hardness and resilience to healthy bone tissue. The elastic nature of the scaffold displayed promising properties for resistance of internal stresses that can be experienced in situ, once implanted. It can thus be confirmed that 3D Bioprinting has significant value in advanced biomaterial design, with optimum properties for site specific controlled drug delivery.

PL-33: AN OVERVIEW ON NANO-LIQUID CHROMATOGRAPHY: MAIN FEATURES AND RECENT APPLICATIONS TO THE ANALYSIS OF NUTRACEUTICAL COMPOUNDS

[1] Fanali,S.,[2] D'Orazio, G., [3] Fanali, C.

[1]PhD School in Natural Science and Engineering, University of Verona, Italy

[2]Institute of Chemical Methodologies, C. N. R. Monterotondo, Rome, Italy

[3]University Campus Bio-Medico, Rome, Italy

Miniaturization has been introduced several years ago in analytical chemistry including also Liquid Chromatography. Nano-liquid chromatography (nano-LC) has been developed and commercial instrumentation is available. The main features

of nano-LC can be summarized as following: low consumption of both mobile phase and sample volumes, high mass sensitivity, high resolution, perfect coupling of the technique with mass spectrometry (MS). The last advantage over conventional LC is due to the low flow rates applied (nL/min). Compounds' separation is carried out in capillaries of thin diameter (10-100 mm) containing a selected stationary phase (SP). The column contains either packed particles or monolithic material, in addition the SP could be bonded or adsorbed on the capillary wall [1, 2].

Aim of this communication is to present the main features of this technique considering its advantages over high-performance liquid chromatography (HPLC) and also the problems related to its practical used especially when analyzing complex matrices. The selection of the appropriate experimental conditions, e.g., mobile phase type (pH, buffer, organic modifier), SP type, flow rate etc. will also be discussed.

Recently nutraceutical compounds have gained special attention in current research in various field such as pharmaceutical, food chemistry, industry etc. Therefore analytical methods have been developed for qualitative and quantitative analysis utilizing LC-MS and recently also nano-LC. Some examples of applications related to the analysis of nutraceutical compounds reported in literature will be presented focusing on the methodological approach [2, 4].

REFERENCES:

1. D'Orazio G., Fanali C., Asensio-Ramos M., Fanali S. (2017). TrAC-Trends in Analytical Chemistry, 96: 151-171.
2. Fanali C., Rocco A., D'Orazio G., Dugo L., Mondello L., Aturki Z. (2015). Electrophoresis 36: 1073-1081.
3. Rocco A., Fanali C., Dugo L., Mondello L. (2014). Electrophoresis 35: 1701-1708.
4. Fanali C., Dugo L., Dugo P., Mondello L. (2013). TrAC-Trends in Analytical Chemistry 52: 226-238.

PL-34: TOWARDS ADVANCED ELECTROANALYTICAL NANOSENSORS: A PROMISING TOOL FOR THE ANALYSIS OF PHARMACEUTICALS

Ozkan, SA.

Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Nanotechnology has become very popular in the sensor fields in recent times. It is thought that the utilization of such technologies, as well as the use of nanosized materials, could well have beneficial effects for the performance of sensors. Nanomaterials have an impact in each and every sphere of human lives, from cosmetics to drug research. The small size, amazing nature, and unique optical absorption properties of nanomaterials make them quite useful for therapeutic applications in the pharmaceutical drug development, selective destruction of cancer cells and their selective assay. Nanoscience deals with the objects whose smallest dimensions range from several nanometers up to 100 nanometers.

MATERIALS AND METHODS:

Nanomaterials exhibit properties that are quite different from those of materials at large scales. The objects under study in nanotechnology are the nanomaterials, also called as nanostructured materials. All materials are composed of grains, which in turn are made of molecules and atoms. Nanomaterials are those having grain sizes in the range of nanometers.

RESULTS:

The unique properties of these different types of nanomaterials have novel electrical, catalytic, magnetic, mechanical, thermal, or imaging characteristics. Hence, they are highly desirable for applications such as in medical, military, and environmental sectors. The currently used nanomaterials could be classified into four types as; carbon based materials, metal based materials, dendrimers, and composites.

CONCLUSIONS:

Using sensitive pulse methods, the electroanalytical studies are more regularly used on industrial, environmental applications and on the drug analysis in their dosage forms and especially in biological samples. The field of micro-electromechanical systems coupled with biosensors and nanosensors will be everywhere in the near future. This studies provides an overview of some of the important and recent developments brought about by the application of electroanalytical nanosensors based nanostructures to nanotechnology for both chemical and biological sensor development and their application examples on pharmaceutical and biomedical area.

REFERENCES:

1. Kurbanoglu S, Ozkan SA, (2018). Electrochemical carbon based nanosensors: A promising tool In pharmaceutical and biomedical analysis, Journal of Pharmaceutical and Biomedical Analysis, 147:439-457.
2. Kurbanoglu S, Uslu B, Ozkan SA, Elsevier, Nanostructures for Oral Medicine, Chapter 28, Carbon based nanostructures for electrochemical analysis of oral medicines, 2017, 885-925, ISBN: 978-0-323-47720-8

PL-35: CONTEMPORARY APPROACH TO EXTRACTION AND ANALYSIS OF BIOACTIVE COMPOUNDS - ANALYTICAL CHALLENGES AND CASE STUDIES.

[1] Ražić, S., [2] Cvetanović, A.

[1]University of Belgrade – Faculty of Pharmacy, Department of Analytical Chemistry, Belgrade, Serbia

[2]University of Novi Sad - Faculty of Technology, Department for Biotechnology and Pharmaceutical Engineering, Novi Sad, Serbia.

INTRODUCTION:

Plants are promising source of biologically active compounds. There are many available techniques for extraction from natural sources. However, bearing in mind a priori knowledge, present requirements, potential risks and principals of green chemistry, the choice becomes very limited. With subcritical water extraction (SWE) we have a possibility to replace toxic organic solvents with benign fluids. Is it so good? In this work a comparison between several extraction techniques was done, based on analysis of flowers of *Chamomilla matricaria* L. (1). In the second case study SWE was applied in analysis of bioactive compounds from leaves, roots and fruits of *Sambucus ebulus* L. (2). The obtained extracts were characterized in terms of biological and chemical fingerprints.

MATERIALS AND METHODS:

Samples: Chamomile Ligulate Flowers and leaves, roots and fruits of Sambucus ebulus L.. Extraction techniques: subcritical water extraction was compared with Soxhlet, ultrasonic-assisted and microwave-assisted extraction. Determination of total phenolics: Folin-Ciocalteu's method. Determination of total flavonoids: Markham' method. Analysis of polyphenolic compounds: UHPLC-DAD-ESI-MS/MS. Quantitative analysis: HPTLC-UV/VIS. Antioxidant activity of extracts was tested using the stable DPPH radical. Antimicrobial activity was tested by microdilution method and cytotoxic activity with several cancer cell lines.

RESULTS:

SWE was proved as an excellent choice in terms of its solvating properties and selectivity. In both case studies the subcritical water extracts exhibited a strong antioxidant power, enzyme inhibitory, antimicrobial, antiproliferative and cytotoxic properties.

CONCLUSIONS:

Contemporary analytical approach, validation of selected methods and confirmation of biological activity of analysed extracts is on a road map for new challenges, new solutions in order to protect human health and environment.

ACKNOWLEDGEMENTS:

This study was supported by a grants of of the Serbian Ministry of Education, Science and Technological Development (III43009, and TR31013).

REFERENCES:

1. Cvetanović A, Švarc-Gajić J, Gašić U, Tešić Ž, Zengin G,, Zeković Z, Đurović S (2017). J of Supercritical Fluids, 120: 32-42.
2. Cvetanović A, Švarc-Gajić J, Zeković Z, Ražić S, Damjanović A, Zengin G, Delerue-Matos C, Moraira M (2018). J. Chem. Technol. Biotechnol. J Chem Technol Biotechnol, 93: 1097–1104.

PL-36: NEW GENERATION OF CARBON–BASED SENSORS IN VOLTAMMETRIC DETERMINATION OF BIOLOGICALLY ACTIVE COMPOUNDS

[1] Skrzypek, S., [1] Brycht, M., [1] Konecka, K., [2] Nosal-Wiercińska, A.

[1] University of Lodz, Faculty of Chemistry, Lodz, Poland

[2] Maria Skłodowska–Curie University, Faculty of Chemistry, Lublin, Poland

INTRODUCTION:

Rapidly increasing progress in the field of the pharmaceutical and biomedical sciences brought in a revolution on human health. New drugs are synthesized and their determination is of high importance. The sensitive determinations in clinical samples at low concentrations along with high selectivity is required to perform successful drug analysis. Until recently, principally spectrophotometric, and chromatographic techniques were applied to pharmaceutical analysis. Nowadays, the modern electrochemical methods are rapidly gaining popularity in the determination of these agents and their metabolites, and at the same time, they are inexpensive and highly sensitive. With the recent significant progress in the electrochemical techniques, the advancements with regard to instrumentation involving the development and application of the range of solid carbon–based electrodes to the detection of pharmaceutical preparations and biological fluids is observed. In this work, the different solid carbon-based working electrode materials were applied in the analysis of drugs (imatinib, teriflunimide, oxolinic acid, and bithionol).

MATERIALS AND METHODS:

Voltammetric measurements were performed using an EmStat USB potentiostat (Palm Instruments BV, The Netherlands) or μAutolab type II potentiostat-galvanostat (EcoChemie, Autolab B.V., The Netherlands). A three–electrode system was used with platinum wire as counter electrode, silver chloride electrode as reference electrode, and a boron–doped

diamond electrode (BDDE, Windsor Scientific Ltd., United Kingdom), a bare egde plane pyrolytic graphite electrode (EPPGE, ALS Company Ltd, Japan) or EPPGE modified with graphene nanoplatelets (GNPs) as the working electrodes.

RESULTS:

The effect of pH on the electrochemical behavior of drugs was studied using DPV or SWV in Britton-Robinson buffer solutions (pH range of 2.0–12.0). The impact of the influence of the DPV or SWV parameters was also tested. Further, the linear calibration curves were constructed, and a biological relevance of the developed DPV or SWV procedures was demonstrated by quantitative analysis of drugs in the spiked human urine samples with satisfactory recoveries. The influence of some interfering compounds and ions was also evaluated, and good selectivities of the proposed procedures was obtained.

CONCLUSIONS:

The electrochemical sensors were applied for the sensitive and selective determinations of imatinib, teriflunimide, oxolinic acid, and bithionol. The sensors provided the excellent results for DPV or SWV determinations of drugs.

PL-37: SOME PERSPECTIVES FOR MARINE BIODISCOVERY IN IRELAND

Olivier, PT.

Marine Biodiscovery, School of Chemistry and Ryan Institute, National University of Ireland Galway (NUI Galway), University Road, H91TK33, Galway IRELAND

Oceans represent an appealing source of curiosity mainly because of the difficulties associated with underwater explorations. In recent years, some scientific landmarks have paved the way for a deeper understanding of the biological and chemical wealth of the Big Blue and today more than ever, the idea that the future of mankind also lies in the marine environment is largely accepted. Since the first explorations of the Commandant Cousteau in the 1960s, the interest towards marine biodiversity has clearly shifted from macro-organisms to the microworld especially when industrial applications industries are sought. Does it mean that no novelty should be expected from the diversity of sponges, cnidarians or other unique sessile invertebrates inhabiting our oceans?

As an introduction, we will show the benefits of a national initiative to foster the development of Marine Biodiscovery in Europe. We will then scrutinize the potential for novelty of remote and underexplored maritime ecoregions with a particular focus on marine invertebrates from the Pacific Ocean. For instance, the interplay between natural product chemists and marine biologists might lead to a better understanding of the systematics and evolution of zoantharians.[1] Then, the interaction between natural product chemists, synthetic chemists and microbiologists can give some important insights into the unknown metabolic pathways of sponge natural products. These scientific data are essential not only for their basic applications in ecology or molecular biology but also because they will contribute to the sustainable applications of marine natural products in industry.

REFERENCE

1. K. B. Jaramillo, M. Reverter, P. O. Guillen, G. McCormack, J. Rodriguez, O. P. Thomas Scientific Reports 2018, 7138

PL-38: DOES ENVIRONMENTAL CADMIUM INCREASE THE RISK OF PANCREATIC CANCER

Matovic, V., Buha, A.

University of Belgrade-Faculty of Pharmacy, Department of Toxicology "Akademik Danilo Soldatović", Belgrade, Serbia

INTRODUCTION:

Pancreatic cancer (PC) is one of the most lethal human cancers and hence, an aggressive worldwide health concern (1). Although profoundly studied, its etiology is still rather scant. Exposure to environmental cadmium (Cd), a ubiquitous metal with well-established toxic and carcinogenic properties, has been hypothesized to one putative cause of PC (2,3). This case-control prospective study determined Cd levels in tissues from pancreatic cancer patients with the aim to determined Cd levels in pancreatic tissue.

MATERIALS AND METHODS:

The cases were a consecutive series of pancreatic tissue excised from 31 patients with no previous occupational exposure to Cd and a histologically based diagnosis of PC, while as controls, pancreatic-tissue samples were taken during routine postmortem examinations from 29 accidental fatalities or subjects who died from a nonmalignant illness. Tissue samples were wet digested and Cd content was assessed using graphite furnace atomic absorption spectrometry.

RESULTS:

Cd content in cancer tissue significantly differed from the content in controls. High concentrations of Cd (1.27-18.64 μg/g) were found in cancerous tissue when compared to control levels (0.27-2.50 μg/g) with median concentration almost 30 times higher in cancer samples. Furthermore, Cd content in cancerous tissue was three times greater than in surrounding non-cancerous tissue ($P<0.05$). Interestingly, Cd levels were significantly higher even in surrounding non-cancerous tissue when compared to the controls. Furthermore, a dose-response relation between

Cd exposure i.e. Cd levels in pancreatic tissue and pancreatic cancer risk was observed, since odds ratio levels were 2.79 (95% CL 0.91-8.50) and 3.44 (95% CL 1.19-9.95) in the third and fourth quartiles of Cd distribution in the population, respectively.

CONCLUSIONS:

Results of this study indicated a significant association between PC development and Cd exposure. However, further investigations are needed to achieve a better understanding of the environmental Cd involvement in PC which could facilitate its prevention, diagnosis, and therapy.

ACKNOWLEDGEMENTS:

This study was partly supported by the Ministry of Education, Science and Technological Development, Republic of Serbia (Project III 46009).

REFERENCES:

1. Hariharan D, Saied A, Kocher HM (2008). HBP, 10:58-62.
2. Chen C, Xun P, Nishijo M, Sekikawa A, He K (2015). Environmental Science Pollution Research, 22: 17465–17474.
3. Amaral AFS, Porta M, Silverman DT, Milne RL, Kogevinas M, Rothman N, Cantor KP, Jackson BP, Pumarega JA, López T, Carrato A , Guarner L, Real FX, Malats N (2012). Gut, 61:1583–1588.

PL-39: DEVELOPMENT OF NEXT GENERATION GALETERONE ANALOGS FOR PROSTATE AND PANCREATIC CANCERS THERAPY

Njar, V.C.O.

Department of Pharmacology, and Center for Biomolecular Therapeutics, Marlene and Stewart Greenebaum Comprehensive Cancer Center, University of Maryland School of Medicine, 685 west Baltimore Street, Baltimore, MD, $^{2}0^{2}01$, USA.

My talk will focus on the development of the next generation galeterone analogs (NGGAs). Galeterone (Gal) progressed into pivotal Phase III clinical trial in patients with metastatic castration-resistant PC (mCRPC) whose tumor cells express splice variant AR-V7 (ARMOR3-SV). However, the recent termination of this trial (due to trial design flaws) and the required 2550 mg/day high therapeutic dose of gal underscores the need to further systematic refinements to enable development of the NGGAs with enhanced efficacies and high therapeutic indices at low dose-administration expected to result in safer, more effective treatments across all stages/forms of PC. During studies to develop NGGAs to modulate androgen receptor (AR/AR-V7) signaling in PC models, we discovered that gal and its new more efficacious analogs (VNPP414 and VNPP433-3β) also effectively target oncogenic eukaryotic protein translation, via modulation of Mnk-eIF4E axis. These compounds suppress oncogenic peIF4E via degradation of Mnk1 and Mnk2. The AR/AR-V7 and Mnk1/2-eIF4E signaling pathways are implicated in PC and pancreatic cancer (pancreatic ductal adenocarcinoma, PDAC) disease progression/metastasis and associated with drug-induced resistance in these two cancers. The properties and mechanisms of action of the lead NGGAs in clinically relevant in vitro and in vivo models of prostate and pancreatic cancers and their translational potential will be discussed.

PL-40: NANOPARTICLES DRUG DELIVERY IN CANCER

Al-Jamal W.T.

Queen's University Belfast, School of Pharmacy, Northern Ireland, United Kingdom

Most cancer chemotherapeutics lack tissue specificity, resulting in many undesirable side effects. Selective drug delivery to tumour tissues could ultimately increase local drug concentrations at the tumour without the need to escalate the administered doses in patients. A wide range of drug delivery systems has been developed to alter the pharmacokinetics of drug molecules, and enhance their tumour targeting. Furthermore, several approaches have been explored to increase drug bioavailability at the site of action, utilising either the unique characteristics of the tumour microenvironment, such as overexpressed enzymes, acidic pH, and hypoxia, or using external triggers, such as heat, ultrasound, and light. This talk will give an overview of the latest nanoparticles that we have developed in our laboratory to enhance the tumour accumulation of anticancer drugs.

ACKNOWLEDGEMENTS:

Dr Al-Jamal's group has been funded by Prostate Cancer UK (CDF-12-002 Fellowship), the Engineering and Physical Sciences Research Council (EPSRC) (EP/M008657/1), and The Royal Society of London (RG2014 R1).

REFERENCES:

1. Hodgins NO, Al-Jamal WT et al. (2017). J Control Release, 256:141-152.
2. Silva V, Al-Jamal WT. (2017). J Control Release, 253: 82-96.
3. Al-Jamal KT, Al-Jamal WT et al. (2013). ACS Nano, 26: 7(3):1905-17.
4. Al-Jamal WT, Ali Z, and Kostarelos K. (2012). Biomaterials, 33(18):4608-17.
5. Al-Jamal KT, Al-Jamal WT et al. (2010). PNAS, 107:3966-3971.
6. Al-Jamal WT, Al-Jamal KT et al (2008). ACS Nano, 2 (3): 408-418.

PL-41: THE FUTURE OF PERSONALIZED MEDICINE: MICROPHYSIOLOGICAL SYSTEMS (ORGAN-ON-A-CHIP) AND 3D-BIOPRINTING

[1,2] Elçin, Y. M.

[1] Tissue Engineering, Biomaterials & Nanobiotechnology Laboratory, Ankara University Faculty of Science, Ankara, Turkey (www.elcinlab.org)

[2] Biovalda Health Technologies, Inc., Ankara, Turkey (www.biovalda.com.tr)

Personalized medicine, also termed precision medicine, is a new type of therapeutic procedure in which treatment is tailored for an individual patient. In this modality, medical decisions, practices, and products are customized to the individual patient based on the predicted response or risk of disease (1,2). This involves harnessing of the individual's genetic and epigenetic information to customize drug therapy or preventive care. Microphysiological systems based on engineered tissue templates (so called the organ-on-a-chip systems) have come into prominence as three-dimensional (3D) microfluidic cell cultures simulating physiological responses and activities of organs/organ systems, and as novel in-vitro multicellular human organism models for toxicology, drug discovery and personalized medicine research (1). It is anticipated that organ-on-a-chip systems will address the challenging pharmacological and physiological gaps between humans, animal models and classical monolayer cultures. Mimicking the conditions of tissues or organ systems is a step forward to multi-organ systems known as the body-on-a-chip. This approach recapitulates organ functions under biomimetic conditions for "micro-organs" inter-connected with microfluidic channels that serve as arterial and venous lines. 3D-Bioprinting systems are used to develop microconstructs having optimal micro-architecture and cell positioning with the aid of biological molecules and cells with a carrier bioink in gel form (3-5). Both technologies demand tissue-engineering expertise, as they involve use of cells, biochemical molecules, and tunable microenvironments. While the ultimate goal of 3D-bioprinting is to engineer personalized human tissues and organs for transplantation, in the current time it is harnessed to develop better functional organ-on-a-chip systems.

REFERENCES:

1. Elçin YM (2017). Editorial. Stem Cell Reviews and Reports, 13(3):319-320.
2. Parmaksız M, Elçin AE, Elçin YM (2018). In: Turksen K (ed). Skin Stem Cells-2nd Ed., MiMB, Springer Nature, USA, DOI 10.1007/7651_2018_147.
3. Lalegül Ö, Elçin AE, Elçin YM (2018). In: Chun HJ, Park K, Khang G. Enabling Cutting Edge Technology for Regenerative Medicine, AEMB, (Eds.), Springer Nature, USA,
4. Ercan H et al. (2018). In: Chun HJ, Park K, Khang G. Novel Biomaterials for Regenerative Medicine, AEMB, (Eds.), Springer Nature, USA
5. Doğan A, Elçin AE, Elçin YM (2017). Current Pharmaceutical Design, 23(6), 903-914.

ORAL PRESENTATIONS

OP-001: ALBUMIN-BASED NANOPARTICULATE DRUG DELIVERY SYSTEMS

Ilem Ozdemir, D., Ozgenc, E., Ekinci, M., Gundogdu, E., Asikoglu, M.

Ege University, Faculty of Pharmacy, Department of Radiopharmacy, Izmir, Turkey

INTRODUCTION:

Nanoparticles (NPs) are colloidal drug delivery systems which have advantages like improving bioavailability, increasing drug resistance time, targeting the drug to a specific location in the body (1) the quality of different HSA batches was analysed by size exclusion chromatography (SEC. The objective of the study is to develop new human serum albumin (HSA) based NPs which can be used as potential radiopharmaceutical drug delivery system.

MATERIALS AND METHODS:

Several process parameters were examined to achieve a suitable size of NP such as dissolution medium, pH, HSA and crosslinker concentration. Briefly, HSA was dissolved in purified water or 10 mM NaCl solution, adjusted to pH 7-9. Under constant stirring, desolvating agent was added drop wisely. After a desolvation process, 8% glutaraldehyde solution was put into the system to induce particle cross-linking. The resulting NPs were purified by centrifugation and particle yield was calculated. The particle size, zeta potential, polydispersity index (PDI) of NPs were measured by using a Zetasizer Nano ZS.

RESULTS:

According to the particle size, zeta potential, polydispersity index (PDI) and particle yield results, the ideal formulation (228,2±49,051 nm, -26,53 ±9,74 mV, 0.138± 0.05) was obtained with 150 mg HSA in 10 mM NaCl, 8mL desolvating agent and 35 µL crosslinker at pH 9.

CONCLUSIONS:

HAS NPs were prepared by modification of a desolvation technique which described previously (2). In our experiments, the effects of varying production parameters on NP properties were studied. Although the interrelationships between the mentioned parameters are complex, pH was found as the most influencing parameter on NP size.

ACKNOWLEDGEMENTS:

This study was supported by Ege University Scientific Research Project Commission (project number: 16/ECZ016). The authors also would like to thank to The Scientific and Technological Research Council of Turkey (TUBITAK 108S083)

REFERENCES:

1. Elzoghby AO et al., (2012). J Control Release 157(2):168–82.
2. Langer K et al., (2003). Int J Pharm 257(1–2):169–80.

OP-002: THE EFFECT OF POLY VINYL PYRROLIDONE AND MACHINE SETTING (DPI) ON THE SKIN PERMEATION OF INDOMETHACIN LOADED TO FILMS BY PEIZOELECTRIC INKJET PRINTER

[1] Arshad, MS., [1] Shahzad, A.,[2] Ahmad Z., [2] Nazari, K., [3] Hussain, A.

[1] Bahauddin Zakariya University, Faculty of Pharmacy, Multan Pakistan

[2] De Montfort University, Leicester School of Pharmacy, Leicester, United Kingdom

[3] University of the Punjab, College of Pharmacy, Lahore, Pakistan.

INTRODUCTION:

The application of inkjet printing has been favoured as a methodology for personalized medication for last one decade (1). The technique is of particular interest for drug delivery to special need groups such as pediatrics where in smaller dose of medicine to be administered (2). This techniques has been evaluated for the properties of substrate affecting the performance of printed drug (3). Purpose of this study was to explore the application of piezoelectric inkjet technology in customized drug delivery to the laboratory animals.

MATERIALS AND METHODS:

Alcoholic solutions of Indomethacin with or without PVP were printed onto polymeric sheets using a commercial Inkjet printer. Drug loading was varied by selecting a different dot per inches (DPI) onto the dermal Patches of 2×2 cm². The printed patched were evaluated for drug morphologies loading in-vitro release and ex-vivo skin permeation and anti-inflammatory effects using hind paw inflammation model.

RESULTS:

Dermal patches 2×2cm² sprayed at 96, 300 and 600 DPI were calculated to contain indomethacin 3.33ug, 32ug and 130.176ug respectively. In vitro release studies showed 60 to 70% of loaded drug was released in the dissolution medium drug release being higher in the patches loaded with drug solution containing PVP. The SEM results revealed that indomethacin loaded from its alcoholic solution crystallized following solvent evaporation while the drug solution with PVP lack or minimally contain drug crystals. The results of drug permeation studies performed through rat skin using modified Franz diffusion cell recorded permeation of 40 to 50% of loaded drug. Patches

demonstrated a significant anti-inflammatory activity as compared to blank films evaluated by hind paw inflammation model.

CONCLUSIONS:

The personalized medication can be achieved by controlling the amount of drug loading through an inkjet printer head by selecting suitable droplet density. Desired Physicochemical form of drug can be achieved by including appropriate excipient in the formulation.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Bahauddin Zakariya University Multan, Pakistan.

REFERENCES:

1. Daly R,. et al. (2015) Inkjet printing for pharmaceutics 494(2):554-67.
2. Preis M, et al. (2015) Int J Pharm.,494(2):578-84.
3. Genina N, et al (2015) Eur J Pharm Biopharm. 2013;85(3, Part B):1075-83.

OP-003: CLINICAL PHARMACY SERVICES IN INTERNAL MEDICINE UNIT

[1] Balli, FN., [1] Kandemir, EA., [1] Kara, E., [1] Demirkan, K., [2] Sain Guven, G.

[1]Hacettepe University, Faculty of Pharmacy, Department of Clinical Pharmacy, Ankara

[2]Hacettepe University, Faculty of Medicines, Department of Internal Medicine, General Internal Medicine, Ankara

INTRODUCTION:

In Hacettepe University Hospitals, clinical pharmacy postgraduate program students participate in clinical visits with physicians and other health care professionals, thus they provide clinical pharmacy services. The treatments of patients were reviewed by pharmacists in order to provide rational drug use and to identify drug related problems. The aim of this study was to explore the role of clinical pharmacist in pharmaceutical care of internal medicine in patients.

MATERIAL AND METHODS:

Hospitalized patients were followed up between 22 December 2017 and 23 February 2018 in the Internal Medicine ward of Hacettepe University Hospitals. The data were collected from patient file, hospital information database (Nucleus®) and via verbal communication with patients and physicians. Three postgraduate students of clinical pharmacy program were participated in clinical visit. They collected data, evaluated patients and provided interventions about problems related to drug therapy.

RESULTS:

In this study, 39 (%46.4) women, a total of 84 patients of whom the median age was 58 years (18-97 years) were included. The most observed admission reason was dyspnea associated with pneumonia, asthma/COPD. Median drug number per patient was 6 (0-21). Pharmacists made 15 recommendations, of those 14 (%93.3) were accepted and 12 (%80,0) recommendations were applied.The recommendations were about drug-drug interactions (n=7), switching drugs (n=3), dose adjustment (n=2), drug-food interactions (n=1), non-treated indication (n=1) and discontinuation of the drug (n=1). Besides that, with the request of physicians, the clinical pharmacists provided information about steroid side effects, usage and interactions of enoxaparin and warfarin, penetration profiles of antibiotics into the bile and interactions between clopidogrel and protein pump inhibitors.

CONCLUSION:

Clinical pharmacy services can improve the patient care, prevent the drug related problems and reduce the workload of physicians. With clinical pharmacy specialists regularly visiting clinics, rational use of drugs can be achieved.

ACKNOWLEDGEMENT

This study was not supported by any sponsor.

REFERENCES:

1. Rotta I, Salgado TM, et al., (2015). Effectiveness of clinical pharmacy services: An overview of systematic reviews (2000-2010). Int J Clin Pharm., 37(5):687-97.
2. IBM Micromedex® Drug Interactions Section, access date: 29.03.2018

OP-004: CLINICAL PHARMACY PRACTICES IN PSYCHIATRY SERVICES AND OUTPATIENT CLINICS

Yalcin, N., Kelleci Cakir, B., Surmelioglu, N., Celiker, A.

Hacettepe University Faculty of Pharmacy, Department of Clinical Pharmacy, Ankara, Turkey

INTRODUCTION:

Problems in drug administration such as dose adjustment, drug/medication adherence, polypharmacy, monitoring of serum levels, drug interactions, adverse effects and complications etc. are very common in psychiatry services and outpatient clinics (1).

MATERIALS AND METHODS:

Between January 2016 and June 2017, 22 patients were consulted to the clinical pharmacist by physicians and nurses working in the psychiatry service and outpatient clinic. The consultations were evaluated whether the recommendation was accepted or refused. Subsequent problems were categorized.

RESULTS:

Twenty-one (95.45%) of the recommendations were accepted by physicians and nurses. When drug-related problems are classified; drug administration time (6, 27.2%), drug administration (4, 18.2%), drug interactions (4, 18.2%), adverse effects (3, 13.6%), inappropriate dosing (2, 9.1%), drug formulation (2, 9.1%) and polypharmacy (1, 4.6%) were determined. When suggestions made to the problems are classified, regulation of drug administration time (8, 36.4%), drug administration form (crushing/ splitting) (4, 18.2%), alternative drug (3, 13.6%), dose adjustment (2, 9.1%), formulation change (1, 4.6%) and clinical follow-up (1, 4.6%) were applied. Three of the consultant patients (3, 13.6%) did not have any problems and no intervention was reported.

CONCLUSION:

Drug-related problems can be minimized and workload of physicians and nurses can be reduced with the contribution of clinical pharmacy services.

ACKNOWLEDGEMENTS:

The authors would like to thank all patients and staff of psychiatry clinics.

REFERENCES:

1. Sadock BJ, Sadock VA, Sussan N (2017). In: Turkcapar H, Ozdel K (ed). Kaplan&Sadock Psikiyatrik İlac Tedavisi. Gunes Tıp Kitabevleri, Turkey, pp 1-24.

OP-005: THE EVALUATION OF PHARMACEUTICAL CARE SERVICES FOR CORTICOSTREOID THERAPY IN COMMUNITY PHARMACIES IN TURKEY

Ertuna, E.

Ege University, Faculty of Pharmacy, Department of Clinical Pharmacy, Bornova – Izmir, Turkey

INTRODUCTION:

Corticosteroids are used in outpatient setting for treatment of various diseases including asthma, chronic obstructive pulmonary disease (COPD), rheumatologic conditions, severe psoriasis, adrenal insufficiency and prevention of host versus graft reactions. Delivery of patient-centred pharmaceutical care by pharmacists ha been shown to improve therapy outcomes for many conditions including asthma, COPD and rheumatologic diseases [1-3]. The purpose of this study was to determine and evaluate pharmaceutical care services provided by community pharmacists in systemic or high-dose inhaled corticosteroid therapy management in Turkey.

MATERIALS AND METHODS:

A self-administered survey was completed by community pharmacists between March and April 2018. Collected data included demographics, self-reported knowledge about corticosteroids, related adverse events, patient counselling and pharmaceutical care activities.

RESULTS:

100 community pharmacists completed the survey. 32% of pharmaceutical care and patient counselling services provided by participating pharmacists was about corticosteroids. Only 46% of the pharmacists agreed/strongly agreed that they have enough knowledge about corticosteroids and their indications. 79% agreed/strongly agreed that the patients did not have enough knowledge about their drugs and/ or therapies. However, 79% of the pharmacists reported that they did not hand out written information to patients about their therapy. Common reasons for patient counselling request about corticosteroids included administration information (85%), adverse events (54%), compliance issues (44%), dietary advice (44%), alternative therapies to corticosteroids (37%), drug interactions (35%), disease information (29%) and preventive measures against adverse events (26%). 76% of pharmacists always/usually gave information about healthy nutrition with calorie and salt restriction to the patients. Only 24% of the pharmacists always/usually informed the patients taking corticosteroids about immunisation and other preventive measures against infection. 71% of the pharmacists warned their patients against detrimental effects of abrupt discontinuation of corticosteroids. Only 19%, 22%, 21% and 36% of pharmacists always/ usually referred the patients to their physician for annual eye exams, cardiovascular risk assessments, diabetes/blood glucose assessment and osteoporosis and bone health assessment, respectively.

CONCLUSIONS:

Pharmacists should be encouraged to keep their knowledge up to date regarding the aforementioned counselling issues in Turkey. Community pharmacists must implement pharmaceutical care interventions more proactively. Supporting counselling services with written information leaflets and improving referral rates to physicians for routine assessments might improve the quality of care. Further studies are warranted to determine the best possible strategy to improve therapy outcomes, patient safety and quality of care.

REFERENCES:

1. Garcia Cardenas V, et al., (2013). Respiratory Medicine 107: 1346-1355.
2. Ottenbros S, et al., (2014). Int J Clin Pharm 36: 336–344.
3. Rowley AK, et al., (2007). AnnPharmacother; 41: 1705-7.

OP-006: EXPRESSION, ACTIVITY AND DRUG INTERACTIONS OF MRP1 IN HUMAN DISTAL LUNG EPITHELIAL CELLS IN VITRO

[1,2] Selo, MA., [2] Springer, L., [2] Nickel, S., [2] Delmas, AS., [2] Ehrhardt, C.

[1]. University of Kufa, Faculty of Pharmacy, Al-Najaf, Iraq

[2]. Trinity College Dublin, School of Pharmacy and Pharmaceutical Sciences, Dublin, Ireland

INTRODUCTION:

Multidrug resistance-associated protein 1 (MRP1) is highly expressed in human lung tissues (1). However, lower MRP1 expression was observed in bronchial biopsies from chronic obstructive pulmonary disease (COPD) patients in comparison to healthy controls (2). The aims of this project were to investigate the expression, subcellular localisation and activity of MRP1 in freshly isolated human alveolar epithelial type 2 (AT2) and type 1-like (AT1-like) cells in primary culture and in the NCI-H441 cell line. Moreover, the effect of inhaled drugs and tobacco smoke extract (CSE) on MRP1 expression and activity was studied.

MATERIALS AND METHODS:

MRP1 expression in AT2 and AT1-like cells from three different patients as well as over the course of 30 passages of NCI-H441 cells was studied using q-PCR and immunoblot. Confocal laser scanning microscopy and cell surface biotinylation were used to confirm transporter localisation. Transporter activity was assessed by bidirectional transport and efflux studies of the MRP1 substrate, 5(6)-carboxyfluorescein (CF). Furthermore, the effect of budesonide, salbutamol and CSE on MRP1 expression and CF efflux were investigated.

RESULTS:

MRP1 protein abundance increased upon differentiation from AT2 to AT1-like phenotype, however, ABCC1 gene expression remained constant. MRP1 was stably expressed in NCI-H441 cells at similar levels to those in AT1-like cells. The transporter was localised to the basolateral cell membranes. Bidirectional transport studies across monolayers of AT1-like and NCI-H441 cells showed MK-571 sensitive net absorption of CF. Budesonide decreased CF efflux at a concentration-dependent manner, without influencing MRP1 expression, whereas salbutamol had no effect. Despite causing a significant increase in MRP1 abundance, CSE exposure resulted in a significant and dose-dependent decrease in CF efflux.

CONCLUSIONS:

MRP1 increases upon transdifferentiation of AT2 to AT1-like cells in primary culture. In AT1-like and NCI-H441 cells, transporter expression levels, localisation and activity are comparable. Thus, the cell line is a useful in vitro model to study MRP1 in distal lung epithelium. Furthermore, budesonide and CSE reduce MRP1 activity in vitro.

ACKNOWLEDGEMENTS:

This study was supported by a grant from FAMRI (CIA130016). M.A.S. is supported by the Iraqi Ministry of Higher Education and Scientific Research.

REFERENCES:

1. Sakamoto A, et al., (2013). J Pharm Sci, 102(9):3395-3406.
2. van der Deen M et al., (2007). J Biochem Mol Toxicol, 21(5):243-245

OP-007: CORRELATION BETWEEN METABOLOMIC PROFILING AND ANTIOXIDANT ACTIVITIES OF METHANOLIC EXTRACTS FROM 8 CULTIVATED MEDICINAL PLANTS

[1] Gonulalan, E.M., [2] Nemutlu, E., [1] Demirezer L.O.

[1]Hacettepe University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

[2]Hacettepe University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Free radicals and reactive oxygen species play an important role on many diseases such as inflammatory disorders and cancer. in this study, we aimed to investigate the antioxidant activity and to evaluate the correlation between metabolomic profiling and antioxidant activity.

MATERIALS AND METHODS:

In this study methanolic extracts of 8 cultivated plant material (Achillea millefolium, A. filipendulina, Mentha piperita, Nigella damascena, N. sativa, Salvia officinalis, Silybum marianum, Echinacea purpurea) are used to determine antioxidant activity. Different assays (ABTS, DPPH, NO, FRAP, CUPRAC) were chosen to investigate different antioxidant mechanisms. Finally univariate, multivariate and correlations analysis were applied to evaluate correlation between metabolomic profiling and antioxidant activity.

RESULTS:

Antioxidant activity results, at 100 µg/mL concentration are (with the order DPPH, ABTS, NO, FRAP (KEAK), CUPRAC (GAEAK)) A. millefolium (1.34, 42.52, 20.19, 188.09, 118.2), A. filipendulina (24.12, 64.29, 22.98, 223.81, 150.39), M. piperita (91.5, 79.76, 31.99, 605.9, 485.39), N. damascena (0, 4.93, 16.46, 83.33, 31.46), N. sativa (0, 11.22, 19.57, 92.86, 13.96), Salvia officinalis (58.89, 84.01, 25.47, 417.24, 389.59), Silybum marianum (0, 7.99, 13.35, 150.57, 72.91), Echinacea purpurea (0, 17.18, 26.09, 141.05,

59.68). Also the metabolomics analysis of eight cultivated plant has been performed by using gas chromatography-mass spectrometry (GC-MS). After deconvolution and aligned of the chromatograms, 279 mass spectral features have been detected and 129 of them were annotated using retention index libraries.

CONCLUSIONS:

It is a fact that synergy and antagonism play an important role of the whole metabolite instead of single metabolite. Therefore, we compared the whole metabolomic profile of different species and antioxidant activity in order to find metabolites that have negative positive activity. We found 12 metabolites have negative correlation between metabolites levels and antioxidant activity, while 69 positive correlation ($r > 0.70$). 15 metabolites are common for positive and no metabolite is common for negative correlation of 8 plants.

ACKNOWLEDGEMENTS:

This study was supported by grants from Hacettepe University Scientific Research Projects (Project No: THD-2016-9171)

REFERENCES:

1. Kanwar JR, Kanwar RK, Burrow H, Baratchi S (2009). Curr Med Chem, 16: 2373–2394.

OP-008: THE AFFECT OF THE RUN TIME OF GC-MS ON METABOLOMIC AND FLUXOMIC ANALYSIS

[1] Eylem, CC., [2] Erikci, A., [2] Yabanoglu Ciftci, S., [1] Kir, S., [1] Nemutlu, E.

[1]Hacettepe University, Faculty of Pharmacy, Department of Analytical Chemistry,Ankara,Turkey

[2]Hacettepe University, Faculty of Pharmacy, Department of Biochemistry,Ankara, Turkey

INTRODUCTION:

In metabolomics and fluxomics, the purpose is to identify and quantify as much as metabolites in a biological system, although, analytes in a metabolomic sample comprise highly complex mixture. GC-MS is one of the most powerful techniques and commonly used in metabolomics studies. The main advantages of GC-MS are its high chromatographic separation power, high peak capacity, reproducible retention times, robust quantitation, high selectivity and sensitivity, and fast compound identification. There has been an increasing interest in reducing running costs and environmental stress in many analytical laboratories as well as in GC-MS analysis. GC-MS uses helium as the carrier gas, which offers high chromatographic resolution at a wide range of flow rates. Morover the other consumables may also reduced with shorter analysis time. In this study, we investigated the effect of analysis time on metabolomic and fluxomic studies as means of addressing the number of mass future detected and repeatability of the method.

MATERIALS AND METHODS:

Metabolomic and fluxomic (^{18}O based labeling for 5 min) analysis were performed on Caco-2 and FHC cell lines. A 200 µL of Caco-2 and FHC cell extracts was evaporated to dryness in a vacuum dryer concentrator and methoxyamineted and derivatized MSTFA with 1% TMCS. Analysis was performed using GC-MS (Shimadzu GCMS-QP2010 Ultra) with DB-5MS stationary phase column (30 m +10 m duraguard × 0.25 mm i.d. and 0.25-µm film thickness). Three different oven temperature programing were used for long run time (60 min), standard analysis time (37 min) and short analysis time (25 min). Once analysis completed, the complex chromatograms were deconvoluted using AMDIS and the retention time correction and data matrixes creation were done using SpectConnect software.

RESULTS:

After deconvolution and aligned of the chromatograms, the mass spectral features have been detected 244, 306 and 305 for short, standard and long run time, respectively. The overall repeatability (RSD %) of the methods was around 25%. The numbers of missing mass features in data matrix were 7.08% for short, 6.58% for standard and 9.21% for long analysis time.

CONCLUSION:

The analysis time effects on untargeted (metabolomic) and targeted (fluxomic) analysis were compared. According to these results, it was found that the long analysis time gave better selectivity and repeatability for fluxomics analysis. For metabolomic analysis, the repeatability and the number of missing mass features were close to for three methods. However, the number of metabolites analysed is 20% higher in normal and long run time methods compare to shorter analysis time. It can be concluded that long runtime can be used for fluxomic analysis and standard run time can be used for metabolomic studies.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (116Z292)

OP-009: COMPARISON OF CHEMICAL COMPOSITION OF VOLATILE OILS BY SPME AND HYDRODISTILLATION OF CYCTOSEIRA BARBATA SEAWEED AND DETERMINATION OF ANTIMICROBIAL ACTIVITY OF SOLVENT EXTRACTS

[1] Yücel, T.B., [2] Korkmaz, B., [3] Fandakli, S., [4] Yucel, M., [1] Cebeci, T.

[1]Giresun University, Espiye Vocational School, Giresun, Turkey

[2]Karadeniz Technical University, Faculty of Pharmacy, Department of Pharmacognosy, Trabzon, Turkey

[3]Avrasya University, Vocational School of Health Services, Trabzon, Turkey

4Sinop University, Faculty of Fisheries, Sinop, Turkey

INTRODUCTION:

Seaweeds are photosynthetic-like plants and either microalgae or macroalgae vegetative organisms. Around of the world, there are approximately 9000 seaweed species, which are broadly classified into three main groups based on their pigmentation: brown (*Phaeophyta*), red (*Rhodophyta*) and green (*Chlorophyta*) seaweeds (1). Also, in Turkey, algae includes about 5000 species and 600 bibliographies and distribution record. Seaweeds have been reported as one of the rich source possessing novel bioactive compounds such as polyunsaturated fatty acids, vitamins, sterols, amino acids and minerals with the variety of biological active such as antitumor, antiviral, antifungal, insecticidal, cytotoxic, phytotoxic and antiproliferative actions (2).

Literature review on the chemistry of seaweeds mentioned the bioactive compounds and biological activity but, at the present time investigations on the composition and structure of biologically active compounds have increased (3). In the literature, there is no published record on the volatile chemical composition by SPME and antimicrobial activity of the solvent extracts of *C. barbata.*

MATERIALS AND METHODS:

In this study, C. barbata, as a brown seaweed was obtained volatile oils by SPME and hydrodistillation and antimicrobial activity tests were done. C. barbata was collected from Akliman location, Sinop coast, Turkey in November 2017, and identified by Ali Karacuha. Antimicrobial activity tests were done according to the literature (4). All test microorganisms were as follows: E. coli ATCC 25922, P. aeruginosa ATCC 27853, S. aureus ATCC 25923, B. cereus 10876, C. albicans ATCC 10231 and methicillin resistant S. aureus.

RESULTS:

The essential oil of C. barbata was identified by SPME and hydrodistillation representing 99.9% and 99.81% of the total oil, respectively. Main component class in SPME analysis; 54.48% hydrocarbon, 18.93% aldehyde; Clevenger extract was found to contain 51.88% aldehyde, 25.23% terpene and terpenoid compounds. According to antimicrobial activity studies exracts of C. barbata showed good activity against S. aureus, MRSA, E. coli.

CONCLUSIONS:

The quantitative and qualitative determination of essential oils of C. barbata showed that major constituents were hydrocarbon (54.48%) and tetradecane (16.38%) in SPME analyses and aldehydes (51.88%) and hexanal (27.27%) in hydrodistillation, respectively.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Giresun University-BAP- 170417-111.

REFERENCES:

1. Miyashita K. et al., (2013). J. of Func. Foods, 5:1507-1517.
2. Sanjeewa K.K.A. et al., (2016). J. of Photochemistry & Photobiology, B: Biology 162:100–105.
3. Agregan R. et al., (2017). Food Research International 99:979–985.
4. Demirel Z. et al., (2009). J. Serb. Chem. Soc. 74(6):619–628.

OP-010: UTILITY OF POLYSACCHARIDE-BASED CHIRAL SELECTORS IN COMBINATION WITH SUPERFICIALLY POROUS SILICA PARTICLES FOR SEPARATION OF ENANTIOMERS IN HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY

[1] Jibuti, G., [1] Chankvetadze, B., [1] Kharaishvili, Q., [2] Farkas, T.

[1]Tbilisi State University, Institute of Physical and Analytical Chemistry, School of Exact and Natural Sciences, Tbilisi, Georgia

[2]Phenomenex Inc., Torrance, CA, USA

INTRODUCTION:

Use of polysaccharide based chiral selectors (CS) in combination with superficially porous silica particles (SPS) was first reported by our group (1). Resulting chiral stationary phase (CSP) showed distinct advantages over columns prepared with fully porous silica (FPS). Later was also shown use of polysaccharide based SPS CSP in nano-liquid chromatography and capillary electro chromatography. For first studies cellulose tris(4-chloro-3-methylphenylcarbamate)

was used as CS, in recent ones, amylose tris(3,5-dimethylphenylcarbamate, (ADMPC) and cellulose tris(3,5-dimethylphenylcarbamate, (CDMPC)(2).

MATERIALS AND METHODS:

Benzoin, trans-stilbene oxide, Tröger's base and Etozoline where used as chiral compounds for this study. ADMPC and CDMPC where used as chiral selectors. 2.8 µm SPS particles where coated by CDMPC while 3.6 µm SPS particles were coated with a ADMPC using method described earlier(1). n-Hexane, 2-propanol and methanol was used as mobile phase. Experiments where conducted on Agilent 1290 Infinity UHPLC system.

RESULTS:

The enantiomers of Tröger's base where marginally resolved on the FPS-based column in contrasts to almost baseline resolved on the column packed with SPS-based CSP, while both CSPs were prepared with the same percentage content (w/w) of chiral selector. This significant difference in resolution was observed along with higher retention time but lower retention factor (k = 0.83) on the FPS-based CSP compared to the SPS-based CSP (observed retention factors for the latter were k1= 0.95 and k2= 1.15).

SPS CSP's showed better separations especially at high speeds of mobile phase (5 ml/min) it is possible to coat small amount of CS on SPS particles to get very fast separations. In case, when 2 % (w/w) ADMPC was coated on 3.6 µm SPS particles, baseline separations of all four tested chiral compounds was achieved under 30 seconds of analysis time.

CONCLUSIONS:

The results of this study indicate that a combination of polysaccharide based chiral selectors with superficially porous silica is a very useful approach for the preparation of highly efficient chiral stationary phases for HPLC enantioseparations. When working with adequate instrumentation the decrease in column performance at higher flow rates is minimal and highly efficient separation of enantiomers can be achieved with the analysis time in the range of 15–30 s.

REFERENCES:

1. Lomsadze K, Jibuti G, Farkas T, Chankvetadze B, (2012). J. Chromatogr. A,1234:50–55.
2. Rocchi S, Fanali S, Farkas T, Chankvetadze B, (2014). J.Chromatogr. A,1363:363–371.

OP-011: BIOLOGICAL ACTIVITIES, PHENOLIC, VOLATILE AND ESSENTIAL OIL COMPOSITION OF CAMPANULA LATIFOLIA L. SUBSP. LATIFOLIA

[1] Korkmaz, B., [2] Fandaklı, S., [1] Barut, B., [1] Yildirim, S., [1] Sener, SO, [3] Ozturk, E., [4] Yavuz, MH, [4] Karaca, HS, [1] Yayli, N

[1]Karadeniz Technical University, Faculty of Pharmacy, Trabzon, Turkey

[2]Avrasya University, Vocational School of Health Services, Trabzon, Turkey

[3]Karadeniz Technical University, Faculty of Health Sciences, Trabzon, Turkey

4Trabzon High School, Trabzon, Turkey

INTRODUCTION:

Campanula latifolia L. is a species of Campanulaceae family and grows in western Asia and Europe, which has a total of 8 genera and 160 species in Turkey (1). In this work, volatile and phenolic constituents, antioxidant and enzyme inhibition of essential oil (EO) and solvent extracts (n-hexane, acetonitrile, methanol and water) obtained from Campanula latifolia L. subsp. latifolia were investigated.

MATERIALS AND METHODS:

The plant (195 g) used in this study was collected from Ataköy-Çaykara, Trabzon (560 m). Essential oil (0.0723 g) of plant (grounded, 132 g) was obtained by Clevenger method (3 h, at -15 °C, cooling bath). Plant (10 g, each) was extracted separately with n-hexane, acetonitrile, methanol and water (15 mL x 3 times, each) and the extracts were combined and evaporated to give 0,1096 g, 0,0540 g, 0,2310 g, and 0,6137 g crude extract, respectively. Phenolic compound analyzes were performed using the Prominence series HPLC apparatus using the previously developed method. Zorbax Eclipse Plus-C18 (150 mm × 4.6 mm, 5 µm) was used as the analytical column. The mobile phase forms methanol (A, 2% acetic acid solution (pH: 2.65) and water (B). The sample injection volume was 20 µL and the flow rate was 1.5 mL / min. The column oven temperature was set at 25 ° C. The photodiode array detector was used at 270 nm wavelength. Comparative volatile organic compound analyses for the essential oil (0.0723 g), SPME (1 g) and SPME of n-hexane extract (0.0896 g) of the plant were made by GC-FID/MS method.

RESULTS:

GC-FID/MS analyzes for EO, SPME, and SPME of the hexane extract of the plant revealed 36, 31 and 36 natural compounds and n-hexanal (23.1%), limonene (44.0%) and 1,2,3-trimethylbenzene (27.4%) were found as major compounds, respectively. Acetonitrile extract showed higher antioxidant activity (266.16 ± 2.94 (IC50 µg/mL, DPPH), 84.77 ± 3.59 (µM QEE/g,

PRAP), 124.02 ± 3.95 (μM BHAE/g, FRAP) than other extracts. In addition, tyrosinase inhibition, acetylcholinesterase and α-glucosidase enzymes activities was highest in acetonitrile and methanol extracts, and the inhibition results were 53.41 ± 0.64, 100.94 ± 3.59 and 30.42 ± 1.04 μg / mL, respectively. Phenolic compounds in solvent extracts were analyzed by HPLC which revealed 7 phenolic compounds in amounts of 0.1-2.2 mg/g, respectively.

CONCLUSIONS:

Limonene (44.0%) found to be major compound in the SPME and 4-hydroxybenzoic acid, vanillic acid, syringic acid, coumaric acid, sinapic acid, benzoic acid and quercetin were the identified phenolic compounds. Acetonitrile extract showed better antioxidant activity than other extracts. α-Glucosidase enzymes activity was highest in methanol extract which was better then used standard.

REFERENCES:

1. Damboldt J (1978). Campanula L. In: Davis, PH. (Ed.). Vol 6, Edinburgh.

OP-012: IN-VITRO EQUILIBRIUM AND KINETIC BINDING STUDIES TO DEMONSTRATING BIOEQUIVALENCE OF SEVELAMER CARBONATE IN COATED TABLETS DOSAGE FORM BY ION CHROMATOGRAPHY

[1] Sarisan, S., [1] Vural, A., [1] Kayar, G., [1] Gokalp, M., [1] Knezevic, Z.

[1]Abdi İbrahim Pharmaceuticals, Research and Development Center, Istanbul, Turkey

INTRODUCTION:

Sevelamer Carbonate is effective for the control of hyperphosphatemia in patients. The efficacy of the drug is determined by measuring the phosphate binding capacity (1). In this study, in vitro equilibrium binding and in vitro kinetic binding studies were performed for test product and reference product to demonstrate the bioequivalence study by determining the phosphate binding capacity by ion chromatography.

MATERIALS AND METHODS:

The equilibrium binding study is considered the pivotal bioequivalence (BE) study and the kinetic binding study is used to support the pivotal equilibrium binding study (2). Starting from published study (3), we developed approach for the in vitro efficacy evaluation of Sevelamer Carbonate. Analyses were performed using validated method by Ion Chromatography. The equilibrium binding study which is performed under conditions of constant time and varying concentrations of phosphate solution was conducted by designing the test and reference products with eight different phosphate concentrations ranged from 1 mM to 40 mM with and without acid pre-treatment. For kinetic binding study, two constant phosphate concentrations at pH 4.0 and pH 7.0 were designed with the test and reference products at eight different times.

RESULTS:

Langmuir binding capacity constant (k2) and affinity constant (k1) were calculated with respect to equilibrium binding study results. The 90% confidence interval for k2 ratio determined by statistical analysis using SAS® statistical software (Version 9.4,SAS Institute Inc, USA). According to FDA Draft Guidance on Sevelamer Carbonate, the 90% confidence interval for k2 ratio meet an acceptance criteria of within 80% to 120% for both pH conditions (2). In the kinetic binding study, the ratio of test product / reference product bound phosphate was compared.

CONCLUSIONS:

The comparative equilibrium and kinetic in vitro phosphate binding study of Sevelamer Carbonate is proved the bioequivalence between reference and test product which developed and produced in Abdi İbrahim R&D center.

REFERENCES:

1. Mazzeo JR et al., (1999). J Pharm Biomed Anal., 19(6):911-915
2. FDA Draft Guidance on Sevelamer Carbonate. Accessed April 8, 2015
3. Yang et al., (2016). Journal of Pharmaceutical Sciences, 105:864-875

OP-013: TOWARD NEW PROBIOTIC PRODUCTS MANUFACTURING: "BACILLUS SUBTILIS AND BACILLUS AMYLOLIQUEFACIENS" ON DIARRHEA

[1] Demirhan, B., [2] Güragac, FT., [1] Er Demirhan, B., [3] Tastan, H., [2] Kupeli Akkol, E.

[1]Gazi University, Department of Food Analysis, Ankara, Turkey

[2]Gazi University, Department of Pharmacognosy, Ankara, Turkey

[3] Gazi University, Department of Biology, Ankara, Turkey

INTRODUCTION:

Diarrhea is defined as frequent and watery defecation syndrome(1), a serious cause of neonate morbidity and mortality (2). It leads to both the water and electrolyte loss, varying depending on age and nutritional factors (3) Various causes, especially infectious diseases, can lead to diarrhea (4) Worldwide, more than 520.000 children under five die each year from diarrhea.(5)

MATERIALS AND METHODS:

In this study, we researched the effects of Bacillus subtilis and Bacillus amyloliquefaciens strains on antibiotic-induced diarrhea model in rats. Within the research, total aerobic mesophilic, total anaerobic mesophilic and total lactic acid bacteria analyses were performed on the stool samples taken from non- diarrheic, diarrheic and probiotic-administered diarrheic rats.

RESULTS:

The number of bacteria found in normal flora and antibiotic-inhibited flora was compared with the number of bacteria found in flora with Bacillus spores added, and it was determined that the latter inhibited the lactase-positive enteric bacteria and Staphylococcus and Micrococcus re-growth but did not prevent resettling of the anaerobic bacteria on the flora. In addition, when the total aerobic mesophilic bacteria counts were compared, it was found that a 2-log increase originated from the Bacillus species.

CONCLUSIONS:

Biological activity and morphometry findings indicated that the probiotic product prepared from the B. subtilis strain was highly effective in the microbial and antibiotic-associated diarrhea. It is therefore believed that significant medical and economic contributions will be provided through this study's complete analysis of the new probiotic product, which can be used in the treatment of various disorders, such as Clostridium difficile infection, irritable bowel syndrome and inflammatory bowel diseases.

REFERENCES:

1. Xiong et al., (2018). Biomedicine & Pharmacotherapy, 98:834–846.
2. Saavedra et al., (1994). Lancet, 15:1046-1049.
3. Mitchell et al., (1973). Gut, 14:348-353.
4. Dinleyici et al., (2012). Expert Opinion on Biological Therapy, 12:395-410.
5. WHO Fact sheet, Updated May 2017. Diarrhoeal disease.

OP-014: SEPARATION OF ENILCONAZOLE ENANTIOMERS IN CAPILLARY ELECTROPHORESIS AND INVESTIGATIONOF STRUCTURE OF SELECTOR-SELECT AND COMPLEXES BY USING NUCLEAR-MAGNETIC RESONANCE SPECTROSCOPY

[1] Chankvetadze, L., [1] Gogolashvili, A., [1] Tatunashvili, E., [2] Sohajda, T., [2] Szemann, J., [3] Salgado, A., [1] Chankvetadze, B.

[1]Institute of Physical and Analytical Chemistry, School of Exact and Natural Sciences, Tbilisi, Georgia

[2]Cyclolab Ltd., Budapest, Hungary

[3]University of Alcalá, Faculty of Pharmacy, Centro de Espectroscopía de RMN (CERMN), Madrid, Spain

INTRODUCTION:

The enantiomer migration order (EMO) of enilconazole in the presence of various cyclodextrins (CDs) was investigated by capillary electrophoresis (CE). Opposite EMO of enilconazole were observed with β-CD and heptakis(2-di-O-methyl-3,6-O-sulfo)-β-CD (HMDS-β-CD) were used as the chiral selectors. Nuclear Magnetic Resonance (NMR) spectroscopy was used to study the mechanism of chiral recognition.

MATERIALS AND METHODS:

All CE experiments were carried out on a CE system from Agilent Technologies (Germany). Fused-silica capillaries were provided by Polymicro Technologies (USA). A Varian NMR System (USA), was used for all NMR experiments. The spectrometer resonance frequency for 1H was 499.61 MHz. Racemic enilconazole, deuterium oxide (D2O), sodium deuteroxide (NaOD, 40% wt.), phosphoric acid (85%), 85% deuterated phosphoric acid were from Sigma-Aldrich (Germany). Native β-CD was kindly provided by Cyclolab (Budapest, Hungary). Heptakis(2,3-di-O-acetyl)-β-CD (HDA-β-CD) was synthesized in our laboratory according to ref. (1).

RESULTS:

On the basis of rotating frame nuclear Overhauser (ROESY) experiments, the structure of an inclusion complex between enilconazole and β-CD was postulated, in which (+)-enilconazole seemed to form a tighter complex than the (-)-enantiomer. This correlates will with the migration order of enilconazole enantiomers observed in CE. No evidence of complexation between enilconazole and HMDS-β-CD could be gathered due to lack of intermolecular NOE interactions. Most likely the interaction between enilconazole and HDMS-β-CD leads to formation of shallow external complex that is sufficient for separation of enantiomers in CE but cannot be evidenced based on ROESY experiment.

CONCLUSIONS:

Opposite affinity of enilconazole enantiomers was observed to native b-CD and its single component derivative HMDS-b-CD based on CE experiment. 1D ROESY experiments showed the formation of an inclusion complex of both enilconazole enantiomers with ²-CD. On the other hand, no interaction of enilconazole with HMDS-²-CD could be detected from 1D- and 2D-ROESY data, although based on the results of CE experiments these interactions are definitely there.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Shota Rustaveli National Science Foundation (Project #217642)

REFERENCES:

1. Takeo K, Mitoh H, Uemura K (1989). Carbohydr. Res., 187:203–221.

OP-015: INVESTIGATION OF CLONAL RELATIONSHIP BETWEEN GRAM NEGATIVE BACTERIA ISOLATED FROM INTESTINAL FLORA AND DIFFERENT CLINICAL MATERIALS OF HEMATOLOGIC MALIGNANCY PATIENTS

[1] Kaskatepe, B., [2] Suzuk, S., [3] Mumcuoglu, I., [4] Ozet, G., [5] Gunes, E.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Ankara, Turkey

[2]National Antimicrobial Resistance Laboratory, Public Health Institution of Turkey, Ankara, Turkey

[3]Ankara Numune Training and Research Hospital, Department of Microbiology, Ankara, Turkey

4Ankara Numune Training and Research Hospital, Department of Hematology, Ankara, Turkey

5Ankara University, Central Laboratory of Biotechnology Institute, Ankara, Turkey

INTRODUCTION:

Infections are the most important cause of morbidity and mortality especially in hematologic malignancy and chemotherapy patients. Especially in patients with febrile neutropenia, it is aimed to reduce mortality with empirically effective and broad spectrum antibiotic treatment. The choice of empirical treatment is of vital important in these patient groups. Escherichia coli, Acinetobacter baumannii and Klebsiella pneumoniae are among the most frequently isolated Gram negative bacteria in neutropenic patients. The aim of this study was to investigate clonal relationship between the potential pathogen Gram negative bacteria isolated from intestinal flora of hematological malignancy patients and the same bacteria isolated during chemotherapy period from infectious clinical material of same patient and to determine whether Rectal swab (RS) sample can be guided for empirical treatment in this patient group.

MATERIALS AND METHODS:

RS samples were obtained from hematologic malignancy patients not yet on chemotherapy or have no infection on chemotherapy period. E. coli was isolated from these samples, and A. baumannii and K. pneumoniae colonization were investigated. The isolates were identified by Maldi-Tof MS (Bruker/ Germany) instrument with using MALDI-TOF MS Bruker Micro ex LT model Flex Control 3.0 software (Bruker Biotyper; Bruker Daltonics, Bremen, Germany). Colistin susceptibility was determined by broth microdilution method. Susceptibilities of bacteria against meropenem (MRM), imipenem (IMP), piperacillin-tazobactam (TZP), cefepime (FEP), ceftazidime (CAZ) were determined with using Gradient test strips and evaluated according to the EUCAST recommendation (1). The clonal relationship between Gram negative bacteria of intestinal flora and infection agents of same patient was investigated by Pulsed-Field gel electrophoresis.

RESULTS:

All isolates are sensitive against colistin. The resistant rates of antibiotics are 39.1 %, 9.4 %, 6.8 %, 35.1 %, 31 %, and 39.1 % for CIP, MRM, IMP, TZP, FEP, and CAZ respectively. Clonal relationship between 30 pairs (RS and clinical isolates) had the same sensitivity profile was investigated with Pulsed-Field gel electrophoresis. Twenty-three (76.6 %) of 30 pairs were found to have a clonal relationship between the bacterial isolates before and after infection.

CONCLUSIONS:

According to our results, it was determined that it can be able to predict with RS samples about possible agents of infection and their antibiotic susceptibility patterns in the management of hematologic malignancy patients.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Scientific Research Projects of Ankara University (15B0237003)

REFERENCES:

1. European Committee on Antimicrobial Susceptibility Testing. Breakpoints tables for interpretation of MICs and zone diameters (v2017).

OP-016: THE USEFUL EFFECT OF B-GLUCAN ON OXIDATIVE AND NEURONAL DAMAGE CAUSED BY GLOBAL CEREBRAL ISCHEMIA/ REPERFUSION IN A C57BL/J6 MOUSE MODEL

[1] Kaya, K., [2] Ciftci, O., [3] Oztanir, M.N., [4] Taslidere, E., [5] Basak Turkmen, N.

[1]Adiyaman University, Faculty of Pharmacy, Department of Biochemistry, Adiyaman, Turkey

2Pamukkale University, Faculty of Medicine, Department of Medical Pharmacology, Denizli, Turkey
[3]Inonu University, Faculty of Medicine, Department of Brain and Neurosurgery, Malatya, Turkey

4Bezmi Alem Vakif University, Faculty of Medicine, Department of Histology and Embryology, Istanbul, Turkey

5Inonu University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Malatya, Turkey

INTRODUCTION:

Stroke is one of the most common causes of death and disability in developing countries (1). Beta-glucans (βg), that have many useful effects on human health, are natural polysaccharides (2, 3). Our aim in this study was to determine useful effect of βg against oxidative and neuronal damage caused by global cerebral ischemia/reperfusion (IR) in stroke imitated mice via surgical operation.

MATERIALS AND METHODS:

A total of 40 mice divided into four equal groups randomly. The groups were named; group 1 (sham operated (SH)), group 2 (I/R), group 3 (βg) and group 4 (I/ R + βg). The group 1 (SH) was kept as control. Bilateral carotid arteries of subjects in group 2 (I/R) and group 4(I/ R + βg) were clipped for 15 min, and the mice in group 4 (I/R + βg) were treated with βg (50 mg/kg/day), while the mice in group 2 (I/R) were treated with only vehicle for 10 days. The mice of group 3 (βg) were treated with βg for 10 days without carotid occlusion.

RESULTS:

Global cerebral I/R significantly increased oxidative stress (TBARS: 11.9±0.92 nmol/g) and decreased members of anti-oxidant defense system (GSH: 184.3±14.1 nmol/ml, CAT: 0.027±0.002 k/mg, SOD:14.60±2.81 U/mg and GPx:154.9±18.3 U/mg) . In addition, I/R caused histopathological damage in the brain tissue (histopathological score:1.57±0.20) . However, βg treatment ameliorated both oxidative (TBARS: 9.32±0.91 nmol/g, GSH: 206.8±15.2 nmol/ml, CAT: 0.030±0.004 k/mg, SOD: 15.23±1.38 U/mg and GPx: 173.7±16.2 U/mg ($P<0.01$)) and histopathological effects of I/R (histopathological score: 0.85±0.14 ($P=0.05$)).

CONCLUSIONS:

Our present study showed that βg treatment significantly ameliorated oxidative and histological damage in the brain tissue caused by cerebral I/R. The useful effects of βg are probably due to its antioxidant and radical scavenging properties. Therefore, βg treatment can be used as supportive care for ischemic stroke patients.

ACKNOWLEDGEMENTS:

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

REFERENCES:

1. Zhao Z, Lu Z et al. (2017). J. Stroke Cerebrovasc. Dis, 26: 1622-34.
2. Kaya K, Ciftci O, et al. (2016). Acta Bras. Cir, 31: 198–205.
3. Gulmen S, Kiris I, et al. (2010). J. Surg. Res, 164: 325–32.

OP-017: A STUDY ON THE DETERMINATION OF MYCOPLASMA HOMINIS PROFILE WITH DIFFERENT METHODS IN SEXUALLY ACTIVE WOMEN, ANTIMICROBIAL RESISTANCE AND TREATMENT

[1] Ozturk S., [2] Yildiz S., [3] Dursun P., [4] Yener Ilce B., [5] Kaymaz O.

[1]Bulent Ecevit University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Zonguldak, Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Ankara, Turkey

[3]Baskent University, Faculty of Medicine, Department of Gynecology and Obstetrics, Ankara, Turkey

4Ankara University, Biotechnology institute, Departmant of Biotecnology, Ankara, Turkey

5Ankara University, Faculty of Science, Department of Bioistatistical, Ankara, Turkey

INTRODUCTION:

Mycoplasma hominis (M.hominis) infections are sexually transmitted and usually associated with urogenital and respiratory system diseases (1, 2). The aim of our study was to detect *M. hominis* in the vaginal and urine samples of sexually active women (SAW) using three different detection methods and to determine antimicrobial susceptibility and resistance after treatment.

MATERIALS AND METHODS:

Both vaginal and urine samples were collected from 110 SAW at the Başkent University Ankara Hospital for Obstetrics and Gynecology Clinic between March 2015 and February 2016. The presence of M. hominis methods in the vaginal and urine samples was detected by in vitro culture, biochemical test

kits, and PCR (3, 4). The antibiotic susceptibility of each sample was also tested using the kits, single and couple tetracycline treatment was given to the patients.

RESULTS:

M. hominis was detected in 72 of 220 (32.7%) samples, out of which 37 showed inconsistent results with the kits and were validated by PCR. The highest susceptibility rate was observed against pristinamycin (100%), followed by 91%, 83% and 75% for doxycycline, tetracycline, and josamycin, respectively. Twenty-five patients treated with tetracycline were followed up after the end of treatment. M. hominis was not observed in 18 cases where the couple received treatment and was re-isolated in the five monotherapy patients.

CONCLUSIONS:

The rate of M. hominis detection was significantly higher in the vaginal specimens compared to the urine specimens. Antibiotic susceptibility tests indicated that the tetracycline group of antibiotics was successful when given as a treatment to couple.

ACKNOWLEDGEMENTS:

We thank the doctors and nurse in Başkent University Ankara Hospital for Obstetrics and Gynecology Clinic. This research was supported by project number 15H0237005 of the Scientific Research Projects Directorate of Ankara University.

REFERENCES:

1. Gerçeker D (1999). Mycoplasma ve Ureaplasma. In: Temel ve Klinik Mikrobiyoloji.1.Öncü basımevi. Güneş kitabevi, pp 595- 602.
2. Boesen T, Fedosova Nu, Kjeldgaard M, Birkelund S, Christiansen G (2001). Protein Science,10:2577- 2586.
3. Daxboeck F, Zitta S, Stadler M, Iro E, Krauser (2005). J Infect, 51(1):54-8.
4. Miranda C, Camacho E, Reina G, Turino J, Rodrigez Granger J, Yetse R, Bautista MF, Garcia M, Alados JC, De La Rosa M (2005). Eur J Clin Microbiol Infect Dis, 24(5):334- 7.

OP-018: MODES OF ACTION OF CYTOTOXICITY OF ALOE-EMODIN ON LEUKEMIA CELLS

[1] Ozenver N., [2] Saeed M., [1] Demirezer LO., [2] Efferth T.

[1] Hacettepe University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

[2] Johannes Gutenberg University, Institute of Pharmacy and Biochemistry, Department of Pharmaceutical Biology, Mainz, Germany

INTRODUCTION:

Rumex acetosella has a long tradition in folk medicine for the treatment of cancer (1). Rumex species were reported to have anthraquinone-rich phytochemical contents in previous studies (2,3). The main anthraquinone aglycones (emodin, aloe-emodin, physcion, rhein), reported to be present in R. acetosella previously (1,4,5). Structural similarities of anthraquinone aglycones to anthracyclines allow to speculate on their possible anticancer activities.

MATERIALS AND METHODS:

In this study, main anthraquinone aglycones and isolated compounds were tested for their cytotoxicities by resazurin reduction and protease viability marker assays. Detection of inducement of reactive oxygen species (ROS), apoptosis and necrosis, DNA damage as well as cell cycle analysis were performed.

RESULTS:

Aloe-emodin as the most cytotoxic compound revealed IC50 values from 9.872 to 22.3 μM in drug-sensitive wild-type cell lines and from 11.19 to 33.76 μM in drug-resistant sublines, was selected to investigate its mechanism against cancer. Aloe-emodin induced S phase arrest, ROS generation, DNA damage and apoptosis. Microarray hybridization revealed a profile of deregulated genes in aloe-emodin-treated CCRF-CEM cells with diverse functions such as cell death and survival, cellular growth and proliferation, cellular development, gene expression, cellular function and maintenance, which was validated by qPCR analysis. COMPARE and hierarchical cluster analyses of transcriptome-wide mRNA expression were examined to predict sensitive or resistant cells in 60 tumor cell lines of DTP (Developmental Therapeutics Programme) (NCI, USA) to aloe-emodin.

CONCLUSIONS:

Aloe-emodin as well as R. acetosella deserve further investigations as possible antineoplastic drug candidates.

ACKNOWLEDGMENTS

This study was supported by The Scientific and Technological Research Council of Turkey (TÜBİTAK) 2214-A scholarship programme.

REFERENCES:

1. Vasas A, Orban-Gyapai O, Hohmann J (2015). J Ethnopharmacol, 175: 198-228.
2. Demirezer LÖ, Kuruüzüm-Uz A, Bergere I, Schiewe HJ, Zeeck A (2001). Phytochemistry, 58(8):1213-7.
3. Demirezer LÖ (1994). Pharmazie, 49(12):936-7.
4. Duke JA (1992). In: Handbook of biologically active phytochemicals and their activities. Boca Raton, Florida: CRC Press.
5. Fairbairn JW, El-Muhtadi FJ (1972). Phytochemistry, 11(1): 263-8.

OP-019: THE RELATIONSHIP BETWEEN CYTOKINE GENE POLYMORPHISMS AND TYPE 2 DIABETES IN A GROUP OF TURKISH POPULATION.

[1] Ates, I, [2] Guvenc, A., [3] Altuner, D.,[1] Karakaya, A.

[1] Ankara University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

[2] Kırsehir City Hospital, Kırsehir, Turkey

[3] Erzincan University, Faculty of Medicine, Department of.Medicinal Pharmacology, Erzincan, Turkey

INTRODUCTION:

Type 2 diabetes is a hyperglycaemic metabolic disease related with the decrease of insulin secretion. Genetic and environmental factors are playing major role in the development of the disease. Relationship between the inflammation generation and diabetic complications has been showed in recent studies. Following the formation of the oxidative stress after the disorder of the lipid metabolism, the levels of the reactive oxygen species (ROS) increase and insulin resistance develops consequently. Cytokines are important in regulation of the homeostatic mechanisms such as inflammation and tissue repair. Thus, variations in their levels and structures can cause several diseases. The single nucleotide polymorphisms (SNP) forming on the cytokine genes increase the risk of disease development. Recent studies showed the relationship between some inflammatory cytokine gene polymorphisms and the development of complication in patients with diabetes. Based on this, our aim was searching and the evaluating the possible relations between the TNF-α (-308), IL-1β (+3953), IL-6 (-174) gene polymorphisms and the development of the complications in a Type 2 diabetic Turkish patient population by using PCR-RFLP method.

MATERIALS AND METHODS:

A total of 150 Turkish individual participants were grouped in three groups as controls, patients with and withoutdiabetic complications consisting of 50 individuals in each. All the patients were selected from the the Diabetes Clinic at the Ankara Training and Research Hospital. 50 patients were free of complications, whereas the others suffered from complications including nephropathy, retinopathy, neuropathy and coronary heart disease. DNA samples of all the subjects were isolated from the blood samples and stored at -200C until the analysis. Genotyping was performed using a polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) technique.

RESULTS:

Due to our data, both TNF-α and IL-1β gene polymorphisms are significantly related with the development of both disease and complications.

CONCLUSIONS:

TNF-α and IL-1β gene variations enhance the risk of Type 2 diabetes and its complications development.

OP-020: RETROSPECTIVE ANALYSIS OF HACETTEPE DRUG AND POISON INFORMATION UNIT –TERATOGENICITY CONSULTANCY SERVICES (HIZBIB-TDS)' DATA ABOUT DRUG USE IN PREGNANTS

[1,2] Celiker, A., [1] Ozdemir, N.

[1]Hacettepe University, Faculty of Pharmacy, Department of Clinical Pharmacy, Ankara, Turkey

[2]Hacettepe Drug and Poison Information Unit-Teratogenicity Consultancy Services-Ankara-Turkey

INTRODUCTION:

Exposure to drugs, radiation, etc in pregnancy can lead to notorious consequences on the fetus. The alarming case reports caused anxiety in both patients and physicians about fetus and drug relationship in 1960s. Eventually, Teratogenicity Consultation Centers have been established all over the world since 1970s to provide information especially for physicians (1). Hacettepe Drug and Poison Information Unit has been in service to give drug information to health care personnel and public also since 1992. HIZBIB started a project in 2015 for providing consultancies to obstetricians in Hacettepe University (HU) about xenobiotics, radiation etc. exposures during pregnancy. After the interviews with the patients referred to HIZBIB, the evaluation reports about the determinants affecting the prognosis of pregnancy were submitted. In this study, it was aimed to evaluate the efficiency of consultancy services provided by HIZBIB-TDS.

MATERIALS AND METHODS:

Between October 2015 and April 2018, 79 patients referred to HIZBIB from HU Faculty of Medicine, Department of Obstetrics and Gynecology were recorded and the descriptive statistical analysis was made retrospectively.

RESULTS:

The range of the ages was 19-41, mean age was 31,54 years. Seventy three pregnants had USG outcome with a range of 4-23 weeks and an average of 8.78. In addition to drugs, other co-agents were radiation (8), herbs (10), kin marriages (4), Rh incompatibility (3), smoking (12), alcohol (3) and illicit substances (2). Antidepressants ranked at first with 22,7 8 % and antibiotics followed them with 21,51%. HIZBIB recommended in 49,36% of pregnants a normal or careful follow-up, in 36,70% warned about a raise in risk for a healthy prognosis, and in 8,86% suggested therapeutic abortus. One month later, the pregnant women were called by telephone and inquired about the current situation; 5 of the 7 abortion proposals (71,42%) had been carried out.

CONCLUSION:

Physicians should be very careful while prescribing during pregnancy and pregnants should also be aware of the probable factors endangering the course of their pregnancies. Being overly cautious or underestimating the situation may lead to negative consequences. HIZBB provides a substantial contribution to the physicians by keeping them as updated, especially in prescribing for pregnants.

ACKNOWLEDGEMENT

We thank to Gulru Gurdemir and Derya Burtul for their valuable contributions in recording and retrieval of data.

REFERENCES

1. De Santis M, et al., (2008). Prenatal drug exposure and teratological risk:One-year experience of an Italian Teratology Information Service. Med Sci Monit, 14(2): PH1-8

OP-021: ANTI-ANGIOGENIC AND TOXICITY EFFECTS OF DERRIS TRIFOLIATA EXTRACT IN ZEBRAFISH EMBRYO

[1] Wan Azizi, WS., [2] Unal, K.

[1] International Islamic University Malaysia, Faculty of Pharmacy, Department of Basic Medical Science, Kuantan, Malaysia

[2] International Islamic University Malaysia, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Kuantan, Malaysia

INTRODUCTION:

Derris trifoliata has been traditionally used as folk for the treatment of, rheumatic joints, diarrhoea, and dysmenorrhea, and rotenoids isolated from the plant have shown to exhibit anti-cancer properties. This study aimed to assess the toxicity effects and antiangiogenic activity of extract of Derris trifoliata on zebrafish embryo model.

MATERIALS AND METHODS:

Zebrafihs embryos were treated with aqueous extract of Derris Trifoliata to evaluate its effects on angiogenesis and zebrafish-toxicity. Angiogenic response was analyzed using whole-mount alkaline phosphatase (AP) vessel staining on 72 hours post fertilization (hpf) zebrafish embryos.

RESULTS:

1.0 mg/ml concentration was toxic to zebrafish embryos and embryos exposed to concentrations at 0.5 mg/ml and below showed some malformations. Derris trifoliata aqueous extract also showed some anti-angiogenic activity in vivo in the zebrafish embryo model wereby at high concentration inhibited vessel formation in zebrafish embryo.

CONCLUSIONS:

The anti-angiogenic response of extract of Derris trifoliata in zebrafish in vivo model suggest its therapeutic potential as anti-cancer agent.

ACKNOWLEDGEMENTS:

This study was supported by a grant of RIGSS (16-291-0455)

REFERENCES:

1. Ito C, et al., (2004). Planta Medica, 70(06):585-588.
2. Khan MR, Omoloso AD, et al., (2006). Fitoterapia, 77(4):327-330.
3. Mamoon SA, Azam M (2011). International Journal of Pharmacy & Life Sciences, 2(9).
4. Mamoon SA, Azam M (2012). International Journal of Pharmaceutical Sciences and Research, 3(1):97.

OP-022: DRUG INTERACTION OF TACROLIMUS AND CYCLOSPORINE IN RENAL TRANSPLANT PATIENTS

Tecen Yucel, K., Ozdemir, N., Aras, E., Bayraktar Ekincioglu, A., Demirkan, K.

Hacettepe University, Department of Clinical Pharmacy, Ankara-TURKEY

INTRODUCTION:

Immunosuppressive drugs are used to prevent organ rejection after transplantation. Most immunosuppressive drugs have narrow therapeutic ranges which increases the risk of clinically relevant drug interactions. The study aimed to assess possible and clinically relevant drug interactions of tacrolimus and cyclosporine individually in patients with renal transplantation (1).

MATERIALS AND METHODS:

A prospective, observational study was conducted in nephrology outpatient clinic at the Hacettepe University Hospitals between November 2017-February 2018. Renal transplantation patients

using tacrolimus or cyclosporine for >1 month were included in the study. A clinical pharmacist attended clinic visits with the physician and evaluated drug interactions. An evaluation of drug interactions was performed using Micromedex© information source and then classified as minor, moderate, major and contraindicated. The change in serum concentration of immunosuppressive drugs by ≥30% was considered as 'clinically significant'. 'Drug Interaction Probability Scale (DIPS) was used to determine drug-drug interactions that thought to be responsible for the change in serum concentration and then evaluated for its clinical significance.

RESULTS:

A total of 93 patients (67 in tacrolimus; 26 in cyclosporine) were included in the study; 52.69% were male and average (±standard deviation) age was 40.1±1.27 years. The median (range) daily drug dose of patients was calculated as 3 mg (1-10) for tacrolimus and 100 mg (50-150) for cyclosporine. In total, 135 potential drug interactions (86 with cyclosporine; 49 with tacrolimus) were identified by a clinical pharmacist; of those 90 were moderate, 41 were major and 4 were contraindicated. The most common drug interaction of cyclosporine and tacrolimus was with prednisolone (n=23; 25.56%) and lansoprazole (n=18;36.73%) respectively. According to the DIPS evaluation; cyclosporine-prednisolone (n= 6), tacrolimus-lansoprazole (n=1), cyclosporine-lercanidipine (n=1), cyclosporine-amlodipine (n=1), cyclosporine-prednisolone-allopurinol (n=1) and cyclosporine-colchicine (n=1) interactions are classified as 'possible'. Although daily doses of immunosuppressive drugs were not too high, the serum concentration of these drugs have been increased. As a result, in order to maintain normal therapeutic range of serum concentrations, dose reduction or drug change was applied where appropriate.

CONCLUSIONS:

The monitoring of possible drug interactions in the treatment process of transplant patients by a multidisciplinary healthcare team that includes a clinical pharmacist, will help to identify and prevent potential drug interactions and to ensure desired outcomes.

ACKNOWLEDGEMENTS:

The authors would like to thank all participating patients and hospital staff at the outpatient clinic.

REFERENCES:

1. Vethe NT, et al, (2011). Drug interactions and immunosuppression in organ transplant recipients. Tidsskr Nor Laegeforen;131(20):2000-3.

OP-023: EFFECTS OF URSOLIC ACID AGAINST STREPTOZOTOCIN INDUCED DIABETES IN WISTAR ALBINO RATS

[1] Bacanli, M., [1] Aydin, S., [2] Anlar, HG.,[1,3] Cal, T., [4] Ari, N., [1] Undeger Bucurgat, U., [5] Basaran, AA., [1] Basaran, N.

[1] Hacettepe University, Department of Pharmaceutical Toxicology, Ankara, Turkey

[2] Bulent Ecevit University, Department of Pharmaceutical Toxicology, Zonguldak, Turkey

[3] KaradenizTechnical University, Department of Pharmaceutical Toxicology, Trabzon, Turkey

[4] Ankara University, Department of Pharmacology, Ankara, Turkey

[5] Hacettepe University, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

Diabetes, a heteregenous metabolic and chronic disease, is a growing health problem in most countries (1). It has claimed that diabetes is associated with the increased formation of free radicals and decreased antioxidant potential (2). Ursolic acid, a well-known pentacylic triterpene which is commonly used in traditional Chinese medicine due to its health beneficial effects (3). The aim of this study was to investigate the effects of ursolic against streptozotocin (STZ)-induced diabetes in Wistar albino rats.

MATERIALS AND METHODS:

DNA damage was evaluated by single cell gel electrophoresis (Comet) assay. Catalase (CAT), superoxide dismutase (SOD), glutathione reductase (GR) and glutathione peroxidase (GPx) enzyme activities and 8-hydroxy-2'-deoxyguanosine (8-OHdG), total glutathione (GSH) and malondialdehyde (MDA), insulin, total bilirubin and bicinchoninic acid (BCA) protein, alanine aminotransferase (ALT), aspartate aminotransferase (AST) and gamma-glutamyl transferase (GGT), high density lipoprotein (HDL), low density lipoprotein (LDL), total cholesterol and triglyceride levels were also evaluated.

RESULTS:

Ursolic acid treatment was found to significantly decrease DNA damage, GR enzyme activities and MDA levels and significantly increase GSH levels and CAT, SOD and GSH-Px enzyme activities and altered lipid and liver enzyme parameters in diabetic rats.

CONCLUSIONS:

According to our results, it seems that ursolic acid might be beneficial against diabetes induced renal damage.

ACKNOWLEDGEMENTS:

This study was funded by a grant from The Scientific and Technological Research Council of Turkey (Project number: 114S919).

REFERENCES:

1. Shaw JE, Sicree RA, et al., (2010). Diabetes Research and Clinical Practice, 87:4-14.
2. Naziroglu M, Butterworth PJ (2005). Canadian Journal of Applied Physiology 30:172-185.
3. Jang SM, Yee ST, et al.,(2009). International Immunopharmacology, 9(1):113-119.

OP-024: A NOVEL OPTICAL BIOSENSOR PLATFORM FOR LABEL-FREE DNA SEQUENCING

Cetin, AE.

Dokuz Eylul University, Izmir International Biomedicine and Genome Institute, Izmir, Turkey

INTRODUCTION:

The demand for cost-effective sequencing drove the development of high-throughput sequencing, e.g., next generation sequencing (NGS). The development of fluorescence-based sequencing platforms dramatically improved the throughput and speed. However, these platforms suffer from problems related to the use of labels such as the complexity and the high cost of labeling, mismatch between number of fluorescence dyes and nucleotides, and photobleaching.

MATERIALS AND METHODS:

In order to address these problems, we introduced a nucleic acid sequencing platform that employs sequencing by binding (SBB) in a label-free biosensing platform. The platform employs gold nanohole arrays that support optical resonances, which are highly sensitive to the presence of the biomolecules on the sensing surface. In the SBB method, immediately before the incorporation of the nucleotide, a complex consisting of the primer-template, polymerase and the correct nucleotide is formed (Figure A). Formation of protein complexes on the sensing surface triggers a spectral shift within the optical resonances supported by the nanohole arrays, and accurately identifies the correct sequence of different DNA templates with high signal-to-noise ratio (SNR).

RESULTS:

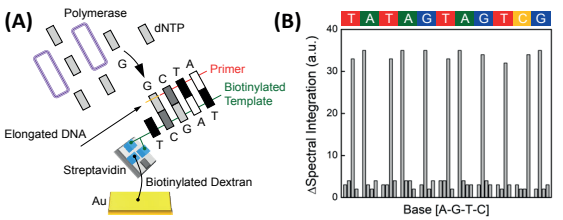
Figure B shows the change in the optical response of the label-free platform due to the formation of protein complexes on the sensing surface for 11 sequencing cycles for a GC50-A DNA template, where the primer. We successfully predicted the correct bases and the spectral variations due to the incorrect bases are negligible. The correct bases yield approximately one order of magnitude larger optical response change compared to the incorrect bases. This distinct signal difference between correct and incorrect interrogation steps demonstrates the reliability of our label-free sensing platform for sequencing applications. We further developed our sequencing platform by integrating it with an imaging based device. In our lens-free platform, we provided the sequencing data by monitoring the intensity variations within the diffraction patterns due to the formation of protein complexes on the sensing surface.

CONCLUSIONS:

Our platform accurately provides sequencing data by detecting protein complexes formed by polymerase mediated pairing of a correct nucleotide with a primed-template DNA resulting in spectral variations within optical resonances. Enabling the utilization of the whole sensing surface for sequencing, our lens-free platform is an ideal candidate for low-cost and high-throughput label-free DNA sequencing applications.

REFERENCES

1. Cetin et al., (2017). ACS Sensors, 3:561-568.



OP-025: ENANTIOSEPARATION OF KETOCONAZOLE ANTIFUNGAL DRUG USING CAPILLARY ELECTROPHORESIS

[1,2] Bounoua, N., [1] Sekkoum, K., [1] Belboukhari, N.

[1]University of Tahri Mohamed, Faculty of Science and Technology, Bioactive Molecules and Chiral Separation Laboratory, Bechar, Algeria

[2]Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Chiral imidazole and triazole derivatives are widely used human and veterinary drugs and also agrochemicals (fungicides) (1), ketoconazole as an important category of antifungal agents, inhibit the synthesis of ergosterol, the essential composition, on the cell membrane to prohibit the growth of fungus (2, 3). Analytical methods used for chiral separations of itraconazole and ketoconazole include several methods, CE has attracted greatly increasing interest for chiral separations (4).

MATERIALS AND METHODS:

the separation of enantiomers of some chiral antifungals was studied by CE. The separation was achieved using heptakis (2, 3, 6-tri-O-methyl)-β-cyclodextrin (TM-β-CD). The influence of TM-β-CD concentration, phosphate buffer concentration, buffer pH, Temperature and applied voltage were investigated. The optimum conditions for chiral

separation of ketoconazole was achieved using 50 mM phosphate buffer at pH 2.5 containing 1-100 mM TM-β-CD with an applied voltage of 30 kV at 15°C with a 3-s injection time (hydrodynamic injection).

RESULTS:

Ketoconazole was successfully resolved. Under described conditions, the increase of concentration leads to an increase of resolution for this we chose 100 mM of Heptakıs (2, 3, 6 tris-O-methyl)-β-CD for this study, it gave the highest resolution for ketoconazole (R= 1.10, α= 1.06) for the first time within 7 min.

CONCLUSIONS:

In this present work the CE method is more selective and rapid to achieve a fast and very efficient separations of variety of antifungals.

ACKNOWLEDGEMENTS:

The authors would like to thank University of Tahri Mohamed Bechar for supplying internship and their financial assistance with this project. And lot of thank for Department of analytical chemistry faculty of pharmacy of Ankara University for Scholarly resources and for providing labs for this work.

REFERENCES:

1. Pyrgaki C, Bannister S, Gera L, Gerber JG, Gal J (2011). Chirality, 23:495–503.
2. Fromtling RA (1988). Clin Microbiol Rev, 1:187–217.
3. Bounoua N, Sekkoum K, Belboukhari N, Cheriti A, Aboul Enein HY (2016). Journal of Liquid Chromatography & Related Technologies, 513-519.
4. Castro Puyana M, Crego AL, Marina ML (2005). Electrophoresis, 26:3960–3968.

OP-026: EVALUATION OF GENOTOXICITY IN TURKISH WELDERS BY COMET ASSAY

[1] Aksu, I., [2] Anlar, HG., [1] Bacanli, M., [3] Iritas, S., [4] Tutkun, E.,[5] Yilmaz, OH.,[1] Basaran, N.

[1] Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Ankara, Turkey

[2] Bulent Ecevit University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Zonguldak, Turkey

[3]The Council of Forensic Medicine, Branch Office of Ankara, Ankara, Turkey

4Bozok Univesity, Faculty of Medicine, Department of Public Health, Yozgat, Turkey

5Yildirim Beyazit Univesity, Faculty of Medicine, Department of Public Health, Ankara, Turkey

INTRODUCTION:

Worldwide, an estimated 11 million workers have a job title of welder, and around 110 million additional workers probably incur welding related exposures. In the present evaluation, welding fumes and UV radiation from welding were classifed as “carcinogenic to humans” (Group 1) (1). The single cell electrophoresis (COMET) assay has been found to be a very sensitive, rapid, reliable and fairly inexpensive way of measuring DNA damage (2). The aim of this study was to investigate the possible genotoxic effects associated with occupational exposure in Turkish welders using COMET assay in lymphocytes and whole blood cells.

MATERIALS AND METHODS:

The study group consisted of 48 male welders. Male office workers (n=48) without any occupational exposure comparable for age and smoking habits to the workers were selected as the control group. Approximately 3 ml whole blood samples were taken and lymphocytes were isolated by Ficoll-Hypaque density gradient procedure (3). The basic alkaline COMET assay of Singh et al., as further described by Collins et al., was performed (4,5).

RESULTS:

DNA damage in the lymphocytes and the whole blood cells of the workers were found to be significantly higher than the control group ($p<0.05$).

CONCLUSIONS:

The findings of increased DNA damage in peripheral lymphocytes and whole blood of welding workers demonstrate the possibility of genotoxic risk. The workers in this study must be examined in detail to avoid the development of a carcinogenic process.

ACKNOWLEDGEMENTS:

This work was supported by Hacettepe University (Grant number: THD-2015-7282).

REFERENCES:

1. Guha N, Loomis D, et al., (2017). The Lancet Oncology, 18(5):581-582.
2. Collins A, Dusinska M, et al., (1997). Environ Mol Mutagen, 30(2):139-146.
3. Boyum, A (1976). Scand J Immunol, Suppl 5:9-15.
4. Collins AR, Dobson VL, et al., (1997). Mutat Res, 375(2):183-193.
5. Singh NP, McCoy MT, et al., (1988). Exp Cell Res, 175(1):184-191

OP-027: THE EVALUATION OF THE PROTECTIVE ACTIVITY OF ANGIOTENSIN II RECEPTOR BLOCKER LOSARTAN AGAINST CISPLATINE INDUCED NEPHROTOXICITY IN MICE

[1] Teke, S., [2] Bayrak, G., [2] Kibar, D., [1] Citak, EC., [2] Yilmaz, SN.

[1] Mersin University, Faculty of Medicine, Discipline of Pediatric Oncology, Mersin, Turkey

[2] Mersin University, Faculty of Medicine, Department of Histology and Embryology, Mersin, Turkey

INTRODUCTION:

Cisplatin is one of the most commonly used antineoplastic agents today. However, especially dose-related and cumulative nephrotoxicity is the most important dose-limiting factor in clinical use (1,2). Our study aimed to demonstrate the role of angiotensin 2 receptor blocker losartan (Los) against cisplatin (Cis) induced nephrotoxicity.

MATERIALS AND METHODS:

15 BALB-C female mice were divided into three groups as control, Cis and Cis + Los groups. Saline was injected to the animals in the control group intraperitonealy (i.p.). A single dose of cisplatin (12.7mg/kg/dose) and after one hour 5 ml of 0.9% sterile saline was injected to the animals in Cis group (i.p.). A single dose of cisplatin (12.7mg/kg/dose) and after one hour 5 ml of 0.9% sterile saline was injected to the animals in the Cis+Los group (i.p). Four days before the injection of cisplatin, losartan (10mg/kg/day) po was started and given for nine days in the third group. On the fifth day after cisplatin injection, all groups were injected with 5-bromo 2-oxyuridine (BrdU, 200mg/kg) and after four hours, kidneys were removed and fixed in formalin. Right kidneys were stained with hematoxylin and eosin (H&E) for morphological examinations. Left kidneys were examined for tubular proliferation and apoptosis by immunohistochemistry. Approval for the study was obtained from the Animal Experiments Local Ethics Committee in Mersin University.

RESULTS:

Glomeruli and tubules had normal morphology in control group. Examination of the Cis group revealed cast formation, thyroidisation, and tubular dilatation. There were locally degenerated tubules and atrophic glomeruli. Congestive changes were also observed. In the Cis+Los group, similar features were observed as in the Cis group but the pathological findings were decreased. For the active caspase-3 labeling, there were very few positive cells in the control group which is increased significantly in the Cis group, while those in the Cis+Los group decreased significantly compared to the Cis group. For the anti-BrdU labeling examinations, positively stained cells were found in the control group which was decreased significantly in the Cis group, and increased significantly in the Cis+Los group.

CONCLUSIONS:

It was concluded that losartan could be used as a protective agent against cisplatin nephrotoxicity. However, further studies are needed to determine optimal doses to maximize its protective effects.

ACKNOWLEDGEMENTS:

This study was supported by the Research Fund of Mersin University in Turkey with Project Number 2016-2-TP3-1947.

REFERENCES:

1. Sobrego A, Guglielmi A et al. (1990) Current strategies to reduce cisplatin toxicity. J Chemother 2:3.
2. Kelland L. (2007) The resurgence of platinum based cancer chemotherapy. Nat Rev Cancer; 7: 573-584.

OP-028: PATIENT-TAILORED PATCH PRODUCTION WITH 3D PRINTER

Azizoglu, E., Serim, I., Arslan Azizoglu, G., Ozer, O.

Ege University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Izmir, Turkey

INTRODUCTION:

3D printing is a novel and revolutionary production technique of our era. Since 3D printing technology makes it possible to manufacture patient-tailored implants and medical devices, studies for personalized treatment are rapidly increasing (1).

Salicylic acid (SA) is one of the most consumed drugs today. In addition to oral route, it is also used for topical keratolytic, bacteriostatic, fungicidal and photoprotective effects. If SA is applied to large surfaces by dermal route, acute salicylate poisoning, in other words salicylism may occur. Therefore, to minimize systemic absorption due to topical application, SA should not be used for long periods and at high concentrations (2).

The aim of this study is to prepare patient-tailored dermal patches for the treatment of acne vulgaris which is one of the most common skin diseases and leaves both physical symptoms and psychological and social problems especially in adolescence, with a modified 3D printer (3).

MATERIALS AND METHODS:

At the first stage, face of the patient was imaged and custom design was made with Fusion 360 software. We then created layers in 2 different combinations with our modified 3D printer (Ultimaker 2, Netherlands). The first layer was composed of PLA layers without active substance as a support layer, whereas the second layer was made with SA solutions. SA solutions were prepared with 2%, 5%, 10% and 20% PVA solutions.

RESULTS:

We have successfully produced patient-tailored patches using the formulation we have selected through our system which we have modified for our studies. By examining the solutions prepared for use in production, 5% PVA and 2% SA containing formulation were considered suitable and patches containing active substance were successfully produced.

CONCLUSIONS:

Patient-tailored patch production becomes easier to implement with our developed production system. Non-toxic and non-irritant production can be made with low-dose, patient-tailored medicines and a more effective treatment can be provided.

Although our study is related to acne vulgaris, there are many illnesses that can be worked with our modified 3D printer. As a result, the system we have developed will be able to produce patient-tailored products for many diseases.

REFERENCES:

1. Stopka et al., (2017). Dynamical Analysis of 3D Printer's Powertrain. Procedia Engineering 192:845-850.
2. Madan RK, Levitt J (2014). Journal of the American Academy of Dermatology, 70(4):788-792.
3. Botros et al., (2015). Evaluation and Management of Acne. Primary Care: Clinics in Office Practice. 42-4:465-471.

OP-029: SYNTHESIS OF CHIRAL SULFOXIDES AND HYDANTOINS AND SEPARATION OF THEIR ENANTIOMERS BY HPLC METHOD

[1] Kakava, R., [1] Konjaria, ML., [1] Shashviashvili, N., [2] Volonterio, A., [1] Chankvetadze, B.

[1] Tbilisi State University, Institute of Physical and Analytical Chemistry, School of Exact and Natural Sciences, Tbilisi, Georgia

[2] Dipartimento di Chimica, Materiali ed Ingegneria Chimica "Giulio Natta", Politecnico di Milano, Italy

INTRODUCTION:

Enantiomeric separation of chiral compounds is extremely important because most of the bioorganic molecules, synthetic drugs and agrochemicals are chiral compounds. Enantiomers in racemic drug compounds are characterized with different biological activities, including pharmacodynamics, pharmacokinetics and toxicology. That is why, enantiomerically pure drug forms are more safe and efficient (1,2). The main goal of the present study was to determine relationships between chemical structure of chiral compound and enantioselectivity in high-performance liquid chromatography.

MATERIALS AND METHODS:

In order to understand the relationships between chemical structure and enantioselectivity, about 50 new chiral sulfoxides and hydantoins were synthezised and their chiral separations were performed with polar organic and normal-phase mobile phases using variety of cellulose based chiral selectors. Majority of these chiral selectors were not described in literature before.

RESULTS:

The main factors contributing in molecular recognition of macromolecules were revealed. Correlation between chemical structure and enantioselectivity was established.

CONCLUSIONS:

Distribution of electron density and geometry of analyte molecules seem to be the major factors affecting enantioselectivity and molecular recognition ability of chiral molecules.

ACKNOWLEDGEMENTS:

This study was supported by Shota Rustaveli National Science Foundation (SRNSF) of Georgia and CNR Italy joint grants (Grants no. 04/02, 2014-2015 and 04/22, 2016-2017

REFERENCES:

1. Branch S. (2001) In. Subramanian, G(ed.) International regulation of chiral drugs. In: Chiral Separation Techniques. A Practical Approach. Weinheim, Wiley-VCH, pp:319-342
2. Chankvetadze B (2012). J. Chromatogr. A, 1269:26-51

OP-030: SYNTHESIS OF NOVEL IMIDAZOPYRIDINES AND THEIR BIOLOGICAL EVALUATION AS POTENT ANTICANCER AGENTS: A PROMISING CANDIDATE FOR GLIOBLASTOMA

[1,2] Guclu, D., [2,3] Kuzu, B., [1] Tozlu, I., [4] Taspinar, F., [5] Canpinar, H., [6] Taspinar, M., [2,3] Menges, N.

[1] Van Yuzuncu Yil University, Faculty of Education, Chemistry Section, Van, Turkey

[2] Van Yuzuncu Yil University, Department of Pharmaceutical Chemistry, Van, Turkey

[3] SAFF Chemical Reagents R&D Lab., YYU-TEKNOKENT, Van, Turkey

[4] Van Yuzuncu Yil University, Faculty of Medicine, Department of Physiology, Van, Turkey.

[5] Hacettepe University Cancer Institute, Department of Basic Oncology, Ankara, Turkey

[6] Van Yuzuncu Yil University, Faculty of Medicine, Department of Medical Biology, Van, Turkey

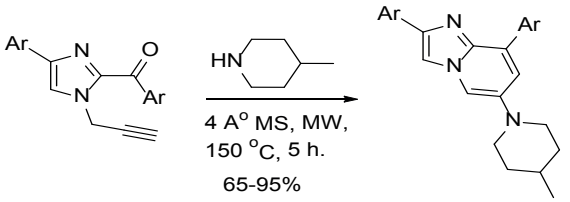
INTRODUCTION:

Gliomas account for approximately 30% of all central nervous system tumors, with glioblastoma being the most aggressive and common type of malignant brain tumor, accounting for approximately 50% of all gliomas.1 The standard treatment for glioblastoma patients is currently surgical resection followed by radiotherapy and/or chemotherapy. The development of chemotherapeutic drug resistance in cancer therapy is an important point that should be considered in the development of new drugs. Imidazopyridine is one of

the most important structural skeletons in the area of natural and pharmaceutical products owing to the broad biological activities of imidazopyridines, such as breast cancer,2 tuberculosis treatment.3 In this work we synthesized new imidazopyridine derivatives with substituents on both imidazole and pyridine rings, and then evaluated their biological activity against a glioblastoma cell line (LN-405).

MATERIALS AND METHODS:

The N-propargyl imidazole derivatives we published in our previous work were used as starting material in this study. These starting materialswere cyclized in a microwave synthesizer using a secondary cyclic amine derivative and molecular sieves.



We used the MTT test to identify the cytotoxicities of the prepared compounds in the first stage of the cell study. To test the antitumor activity, we evaluated the activity of compounds against a glioblastoma cell line (LN-405).

RESULTS:

Various imidazopyridine derivatives bearing different functional groups have been synthesized and their cytotoxicities against a glioblastoma cell line (LN-405) were investigated experimentally.

CONCLUSIONS:

Two lead compounds with IC50 values of 10 and 75 μM were identified for glioblastoma. Pharmacomodulation of these compounds and their structure–activity relationship are currently under investigation, which will hopefully reveal a new promising candidate for glioblastoma.

ACKNOWLEDGEMENTS:

This study was funded by Scientific and Technologic Research Agency of Turkey (TÜBİTAK) (grant numbers:115Z894)

REFERENCES:

1. Bastien JIL, McNeill KA, et al., (2015). Cancer. 121: 502-516.
2. Kamal A, Reddy JS, et al., (2010). Med Chem Commun. 1: 355-360.
3. Pethe K, Bifani P, et al., (2013). Nat Med. 19: 1157-1160.

OP-031: H2S FORMATION IN LIVER IS INDUCED BY ZMP17 AND ZMP20

[1] Yetik Anacak, G., [1] Alancay, E., [1] Sevin, G., [2] Jakopin, Ž., [2] Tomašič,T.

[1] Ege University, Faculty of Pharmacy, Department of Pharmacology, Izmir, Turkey

[2] University of Ljubljana, Faculty of Pharmacy, Aškerčeva 7, SI-1000 Ljubljana, Slovenia

INTRODUCTION:

Hydrogen sulfide (H_2S) is getting attraction as a new therapeutic target in hepatoprotection through anti-oxidative, anti-inflammatory, cytoprotective and anti-fibrotic actions (1). The novel gasotransmitter H_2S is synthesized from L-cysteine by 3 enzymes whose expressions are mostly in liver; cystathionine-β-synthase (CBS), cystathionine-γ-lyase (CSE) and 3-mercaptopyruvate sulfurtransferase (3MPST) [2]. Resveratrol (RVT) has a potential as a hepatoprotective agent (3). We have shown that RVT induces H_2S synthesis (4). However it is not clear whether H_2S formation in liver could be induced by RVT derivatives. Thus we have synthesized new RVT derivatives and investigated the effects of RVT analogues ZMP-17 and ZMP-20 on the formation of H_2S in the liver.

MATERIALS AND METHODS:

The effect of ZMP 17 and ZMP 20 (10 μM, 30 minutes) on basal (L-cysteine free) and stimulated H2S formation by the substrate L-cysteine and cofactor pyridoxal phosphate(10 and 2mM, respectively) in the presence or absence of CSE and CBS inhibitor aminooxyacetic acid; AOAA (10 mM,10 min before ZMP17 or ZMP20 treatment) in mouse liver homogenates were measured by an amperometric H2S microsensor for 30 minutes at 37°C(UnisenseA/S,Aarhus, Denmark).

RESULTS:

ZMP 17 and 20 were synthesized in Lubiana University [5]. ZMP17 or ZMP 20 did not raise the signals in PBS without biological sample, suggesting that it is not an H2S donour. L-cysteine stimulated H2S formation and AOAA inhibited it it significantly, confirming endogenous H2S synthesis in liver. ZMP17 and ZMP20 increased L-cysteine-induced endogenous H2S formation which were reversed back by H2S synthesis inhibitors.

CONCLUSIONS:

We found that ZMP-17 and ZMP-20 induces endogenous H2S formation in liver. Since H2S has been found to be beneficial in liver degeneration (1) the beneficial effect of RVT in hepatoprotection (3) might be related with induction of H2S synthesis.

ACKNOWLEDGEMENTS:

We thank Turkish Scientific Research Council TUBITAK for the grant #114S448,and COST action CA15135.

REFERENCES:

1. Tan G et al. (2011).PLoS One, 6(10):e25943.
2. Wang R (2012).Physiological Reviews, 92(2): 791-896.
3. Faghihzadeh F et al. (2015).Journal of Research in Medical Sciences, 20(8):797-810.
4. Yetik-Anacak G et al. (2015).The Journal of Sexual Medicine, 12(10):2004-12.
5. Gobec, M et al. (2015).Chemico-Biological Interactions, (240):200-7

OP-032: MAY TEUCRIUM MULTICAULE HAVE A ROLE IN PROTECTION OF CCL4 INDUCED LIVER DAMAGE IN RATS?

[1] Yalcin, A., [2] Yumrutas, O., [3] Kuloglu, T., [4] Pehlivan, M., [5] Uckardes, F., [2] Bozgeyik, I., [6] Parlar, A., [7] Yilmaz, I., [8] Dogukan, M., [9] Aydin H., [8] Uludag, O.

[1] Adiyaman University, Faculty of Medicine, Dep. of Histology and Embryology, Adiyaman, Turkey.

[2] Adiyaman University, Faculty of Medicine, Dep. of Medical Biology, Adiyaman, Turkey

[3] Firat University, Faculty of Medicine, Dep. of Histology and Embryology, Elazig, Turkey

[4] Gaziantep University, Nurdagi Vocational Higher School, Dep. of Medical and Aromatic Plants, Gaziantep, Turkey

[5] Adiyaman University, Faculty of Medicine, Dep. of Biostatistics and Medical Informatics, Adiyaman, Turkey

[6] Adiyaman University, Faculty of Medicine, Dep. of Pharmacology, Adiyaman, Turkey

[7] Inonu University, Faculty of Pharmacy, Dep. of Pharmacology, Malatya, Turkey

[8] Adiyaman University, Faculty of Medicine, Dep. of Anesthesiology and Reanimation, Adiyaman, Turkey

[9] Adiyaman University, Faculty of Pharmacy, Dep. of Pharmaceutical Toxicology, Adiyaman, Turkey

INTRODUCTION:

Liver is the largest gland that performs important metabolic functions in the human body and its treatment is a difficult process. The liver diseases remain a problem across the world, and many studies have been continued to search to find the new treatment agents. The synthetic drugs have been used to treat lots of diseases, but it is known that they have a side effect, and so many people have been used the plant and plant extraction to treat some disease for a long time. In this study, hepatoprotective effects, cytotoxic potentials and antioxidant activities of *Teucrium multicaule* Montbret Et Aucher Ex Bentham have been investigated in CCl4 induced liver damage.

MATERIALS AND METHODS:

By using male rats, groups (n:6) were designed as following; control, CCl4, CCl4+200mg/ml T. multicaule MeOH extract and CCl4+400 mg/ml T. multicaule MeOH extract. CCl4 induced liver damage was generated during 7 days. The others groups were administered with 200mg/ml and 400mg/ml T. multicaule extract for seven days. In end of the study, rats were sacrificed and livers were removed. mRNA levels of SOD, CAT and GPx antioxidant enzymes and MDA levels in liver tissues were determined. Apoptotic protein Bax and Caspase 3 levels were determined by immunohistochemical staining, and apoptotic index was estimated by tunnel method. Cytotoxic effect of the extract on murine LR 7 cell was determined as well. Antioxidant activity of the extract was determined by using in vitro method DPPH (1).

RESULTS:

When compared to control and CCl4 group, mRNA expression levels of SOD, CAT and GPx decreased ($p<0.05$). While the expression of Bcl2 was decreased, which of Caspas3 did not change when compared to all of the groups. Immunohistochemically, when compared to CCl4 group, a reduction in expressions of Bax and Caspas3 was detected both in dose of 200 mg/ml and 400 mg/ml of T. multicaule extract ($p < 0.05$). It was observed that the high dose of the extract exhibited a cytotoxic effect on murine LR7 cells. The extract also exhibited a strong antioxidant activity in a dose-dependent manner.

CONCLUSIONS:

Consequently, it is determined that T. multicaule have a strong hepatoprotective activity in CCL4-induced liver damage as well as its antioxidant and cytotoxic activities

ACKNOWLEDGEMENTS:

This study was supported by the Scientific Research Projects Coordination Unit of Adiyaman University (TIPFBAP/2014-0008).

REFERENCES

1. Gaulejac NSC, Provost C, Vivas N (1998). J. Agri. Food Chem., 47:425-431.

OP-033: THE COMPARISON OF DIFFERENT DOSES OF ALOE VERA AND THE BURN DRUGS ON BURN MODELS OF RATS

[1] Macit, C., [1] Tatlipinar, ME., [1] Caglar, ES.,[1] Taner, N., [1] Turgut, S., [1] Sarikaya, EG.

[1] Istanbul Medipol University, School of Pharmacy, Department of Pharmacology, Istanbul, Turkey

INTRODUCTION:

Burn injuries may have serious traumatic consequences.the degree of tissue damage depends on the degree of heat and duration of contact. There are 4 levels of burns (1). Herbal treatments could be applied for alleviating the symptoms in addition to pharmacological treatments. *Aloe vera* is used for burn wounds for many years because of its antiinflammatory, antiviral, antifungal, antibacterial and rapid burn wound healing effects (2). Aim of this study was to compare different doses of *Aloe vera* gel with burn medications in the market.

MATERIALS AND METHODS:

48 female Sprague-Dawley rats divided into 8 groups (negative control, positive control, Silverdin®, Bepanthol®, Sudocrem®, Aloe vera 30 mg, Aloe vera 60 mg, Aloe vera 90 mg). The back of the rats were exposed to 90oC hot water for 10 seconds (burnt area: 7,069 cm2). After the modelling, serum physiologic was applied to each rat. Their treatments were always given at the same time. Experimental study was approved by Istanbul Medipol University Animal Experiments Local Ethical Committee. Obtained data were evaluated with SPSS v21 program.

RESULTS:

After 15-day-treatment, 30 mg of Aloe vera was more effective than Silverdin® cream (Aloe vera decreased burnt area: 3,064 cm2, Silverdin® decreased burnt area: 3,731 cm2). The most effective drug among these medications was Sudocrem® with decreased burnt area 2,302 cm2.

CONCLUSIONS:

It could be concluded as Sudocrem® is the most effective drug when compared to the medications for burn treatment. Furthermore, 30 mg dose of Aloe vera is more effective than Silverdin® cream.

ACKNOWLEDGEMENTS:

This study was supported by a grant of MEDITAM

REFERENCES:

1. American Burn Association/American College of Surgeons (2007). J Burn Care Res, 28:134-41.
2. Rosca-Casian O, Parvu M, Vlase L, Tmas M (2007). Fitoterapia, 78:219-22.

OP-034: ANTIEPILEPTIC ACTIVITY OF FOUR SELECTED SKULLCAP (SCUTELLARIA) SPECIES ON MICE.

[1] Arihan, O., [2] Yildiz Yilmaz, G., [3] Cicek, M.,[4] Demirkol, H.

[1] Van Yuzuncu Yil University, Faculty of Medicine, Department of Physiology, Van, Turkey

[2] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

[3] Pamukkale University, Faculty of Science and Literature, Department of Biology, Denizli, Turkey

[4] Van Yuzuncu Yil University, Faculty of Medicine, Van, Turkey

INTRODUCTION:

Epilepsy is a disorder of central nervous system and has different types. Modern treatment against convulsions includes drugs and surgical treatments (1). Since some of the patients still have convulsions although they are administered with antiepileptic drugs, new molecules are needed (2). Plants have been offered as new candidate molecules in this regard (3). Thus, in this study, we aimed to test anticonvulsive activity of four different Skullcap (Scutellaria) species.

MATERIALS AND METHODS:

Scutellaria brevibracteata Stapf subsp. brevibracteata, S. galericulata L., S. megalaspis Rech.f. and S. orientalis L. subsp. pichleri (Stapf) J.R.Edm. methanolic extracts (aerial parts) were tested on mice in pentylentetrazol induced convulsions. Mice were administered with 200 mg/kg i.p. plant extracts dissolved in physiological saline for 5 days. 80 mg/kg pentylentetrazol was injected in the last day to all groups. Pentylentetrazol group was administered solely with pentylentetrazol.

RESULTS:

Number of animals having tonic clonic convulsions ($p>0.05$) and number of ex animals due to convulsions ($p>0.05$) were decreased after treatment. The latency for tonic-clonic convulsions ($p>0.05$) in all tested Scutellaria groups was increased. A marked increase in latency for first myoclonic convulsion ($p<0.05$) in S. orientalis L. subsp. pichleri (Stapf) J.R.Edm. was observed against pentylentetrazol induced convulsions.

CONCLUSIONS:

The present study may suggest a potential anticonvulsive activity of tested Scutellaria species. Further studies are needed to determine the molecules that are responsible for this activity.

REFERENCES:

1. Moshi MJ, Kagashe GA, Mbwambo ZH (2005). Journal of Ethnopharmacology, 97:327-36.
2. Engel J Jr (1996). American Journal of Neuroradiology, 17:243-4.
3. Singh B, Singh D, Goel RK (2012). Journal of Ethnopharmacology, 139: 273– 279.

OP-035: ENHANCEMENT OF ORAL BIOAVAILABILITY OF POORLY SOLUBLE DRUG TAMOXIFEN THROUGH COMPLEXATION WITH DIFFERENT CYCLODEXTRINS

[1] Erdogar, N., [2] Teksin, ZS., [3] Nemutlu, E., [4] Iskit, AB., [1] Bilensoy, E.

[1]Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

[2]Gazi University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

[3]Hacettepe University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

4Hacettepe University, Faculty of Medicine, Department of Pharmacology, Ankara, Turkey

INTRODUCTION:

Tamoxifen (TMX) is used clinically as a nonsteroidal antiestrogen for first-line endocrine treatment as well as adjuvant therapy in metastatic breast cancer. TMX, a BCS class II drug, shows low plasma drug levels leading to therapeutic failure due to low aqueous solubility. Hence, there is need to develop a new formulation of TMX which can minimize the side effects. Complexation with cyclodextrins is an effective pharmaceutical technique to enhance the bioavailability of poorly soluble substances. The aim of this study is to evaluate in vitro/in vivo properties of cyclodextrin complexes and to improve solubility and oral bioavailability tamoxifen with water soluble cyclodextrins.

MATERIALS AND METHODS:

Tamoxifen citrate (MW: 371.51 g/mol) was kind gifts from TEVA Pharmaceuticals, Israel. Methyl-β-cyclodextrin (M-β-CD) and hydroxypropyl-β-cyclodextrin (HP-β-CD) were supplied as Cavasol® W7M and Cavasol® W7HP respectively, as kind gifts of Wacker Chemie, Germany. Sulfobutyl ether β-cyclodextrin (SBE7-β-CD) was supplied as Captisol®, as kind gift of Cydex Inc. (Lenexa, KS). The inclusion complexes were prepared by two methods (kneading and co-liyophilization) using different CD derivatives and characterized by different techniques including fourier transform infrared spectroscopy, differential scanning calorimetry and scanning electron microscopy. The in vitro properties of tamoxifen as a drug-cyclodextrin inclusion complex were evaluated with solubility and dissolution studies. Oral bioavailability studies were carried out with tablet formulation of tamoxifen with M-β-CD and commercial tablet formulation (Tamoxifen-TEVA).

RESULTS:

The results showed that co-liyophilization method comprises true inclusion complexes between TMX and both cyclodextrins. A dissolution study showed that the solubility and dissolution rate of TMX were significantly enhanced by complexation with M-β-CD. Tablet formulation using 1:1 co-liyophilization complex of TMX and M-β-CD with drug equivalent to 10 mg was prepared by a direct compression method. A dissolution study of prepared tablets was performed in 0.02 N HCl medium. 99% drug was released from the formulation at the end of 30 min. From the comparative results of dissolution study, it was found that the prepared formulation showed better release than a commercially tablet formulation. Tablet formulation of tamoxifen with M-β-CD and commercial tablet formulation (Tamoxifen-TEVA) were administered to male Sprague–Dawley rats by oral gavage. The oral bioavailability of tablet formulation containing TMX/M-β-CD inclusion complex in mice was effectively increased 2-fold over commercial tablet.

CONCLUSIONS:

Complexation of TMX with M-β-CD results in a more efficient tablet formulation with improved dissolution and an enhancement oral bioavailability of the drug.

OP-036: A STUDY ON CURRICULUM DEVELOPMENT OF A COMMUNICATION AND COUNSELING SKILLS COURSE FOR PHARMACY STUDENTS: A SIMULATION BASED APPROACH

[1] Gulpinar, G., [1] Ozcelikay, G.

[1] Ankara University, Faculty of Pharmacy, Department of Pharmacy Management and History, Ankara, Turkey

INTRODUCTION:

The aim of this thesis study is to develop a “Pharmacist-Patient Communication and Counseling Skills” lecture-laboratory course and to determine the impact of this course with standardized patients (SPs) on pharmacy students.

MATERIALS AND METHODS:

The course was a 14-week educational interventional study done at Ankara University Faculty of Pharmacy. A single group pre-test, post-test trial was conducted with the fifth-year pharmacy undergraduate students (n=21). Student SP encounters were assessed by Patient-centered Communication Tools (PaCT) that was adapted to Turkish (1). A two-facet generalizability study was performed to investigate the reliability of the

instrument. The impact of the course was assessed by comparing pre- and post-test scores. Additionally, qualitative data were collected on evaluating the laboratory at the end of the course by a survey.

RESULTS:

Students had significantly higher final assessment scores across all subsections in the instrument ($p \leq 0.001$). The greatest improvements were seen in "demonstrate interest and empathy". Students reported general satisfaction with the content and format of the course and the assessment process.

CONCLUSIONS:

The improvement in demonstrating empathy has come from the understanding of patient centeredness that was underlying the course (2). Additionally, as a recommendation, the course should be designed as spiral curriculum rather than 14-week to enhance the development of students' communication and counseling skills.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Scientific Research Projects Coordination Unit of Ankara University (16L0237003)

REFERENCES:

1. Grice GR et al., (2007). American Journal of Pharmaceutical Education, 81(8):5927.
2. Benbassat J, Baumal R (2004). Academic Medicine, 79(9):832-839.

OP-037: GENOTOXICITY, ANTIOXIDANT ACTIVITY, TOTAL PHENOLIC AND FLAVONOID CONTENTS OF EIGHT RESEDA L. (RESEDACEAE) SPECIES FROM TURKEY.

[1] Zare, G., [1] Arituluk, Z.C., [2] Emecen, G., [2] Cilden, E.

[1]Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

[2]Hacettepe University, Faculty of Science, Department of Biology, Ankara, Turkey

INTRODUCTION:

The genus *Reseda* L. is represented by 15 species in Turkey which 7 of them are endemic (1). *R. lutea* L. is known as a folk medicine and *R. luteola* L. as a dyeing plant due to its high flavonoid content. Flavonoids, due to their strong anti-oxidative potential, might be the subject of interest for developing anti-photoageing, anti-cancer strategies and cosmetic products (2). Thus, we investigated total flavonoid and phenolic contents, antioxidant and genotoxic effect of 8 species to find more effective alternative natural resources.

MATERIALS AND METHODS:

In this study, 5 species consisting of R. alba L., R. aucheri Boiss., R. luteola, R. lutea, Reseda orientalis (Müll.Arg.) Boiss. and 3 endemics consisting of; R. balansae Müll.Arg., R. coodei Hub.-Mor., R. tomentosa Boiss. were investigated. To assess the antioxidant activity, methanol extracts of the aerial parts were prepared and examined by DPPH, ABTS, CUPRAC and FRAP assays. Moreover, total phenolic contents were measured by Folin-Ciocalteu's reagent and their flavonoid contents were measured by aluminum chloride colorimetric methods (3). To test the genotoxicity, The Somatic Mutation and Recombination Test- SMART in Drosophila melanogaster was applied. To determine the potential genetic toxicity of these taxa, the larvae–adult viability was measured in 100 larvae in different 6 concentrations (4).

RESULTS:

For the methanol extracts of Reseda species, the DPPH, ABTS, CUPRAC and FRAP assays revealed comparable results with various potencies. Three species of R. luteola, R. lutea and R. tomentosa in all methods demonstrate significant antioxidant activity compare with the other taxa. R. luteola have the high level of total phenolic *(104.31 mg gallic acid equivalents/g extract)* and flavonoid *(262.88 mg quercetin equivalents/g extract)* contents that provided more evidence to their antioxidant activity. No significant toxic effects and morphological changes were observed for none of the Reseda extracts.

CONCLUSIONS:

Various Reseda species extracts show positive antioxidant activities, however doesn't show any potential toxicity on larvae. Also R. luteola and R. lutea as widespread and R. tomentosa as an endemic species can be recommended as plants with antioxidant activity.

REFERENCES:

1. Davis PH (1975). Flora of Turkey and the East Aegean Islands, Vol.5, University Press, Edinburgh.
2. Seelinger G, Merfort I, Schempp CM (2008). Planta Med., 74 (14): 1667-1677.
3. Arıtuluk ZC, Tatli Çankaya İİ, Gençler Özkan AM (2016). FABAD J Pharm Sci., 41: 17-25.
4. Graf U, Abraham SK, Guzmán-Rincón J, Würgler FE (1998). Mutat Res., 402: 203-209.

OP-038: INVESTIGATION OF THE RELATIONSHIP BETWEEN CHRONIC MONTELUKAST ADMINISTRATION AND DEPRESSION IN MICE.

Telli, G., Bozkurt, TE., Tel, BC.

[1] Hacettepe University, Department of.Pharmacology, Ankara, Turkey

INTRODUCTION:

Montelukast is a leukotriene receptor antagonist which is widely used in inflammatory diseases of the respiratory tract such as asthma prophylaxis and treatment. Although many of the guidelines recommend montelukast (1), many neuropsychiatric side-effects of montelukast especially in children have been reported in recent years. In 2008, FDA has issued a warning about these side-effects of montelukast and recommended that patients should be informed for them. However, these neuropsychiatric side-effects have been poorly investigated and the results were contraversial (2). Although some significant cases have been reported, animal studies are lacking about the relationship between depression and montelukast treatment. In this study, we investigated the effect of chronic montelukast treatment on depression in mice.

MATERIALS AND METHODS:

Porsolt's forced swim (PFST) test was used for the assessment of depression like behavior. Swiss mice (8-12 weeks) from both sex were used in the experiments (Hacettepe University Animal Experimentations Local Ethics Board (2018-3/2). Montelukast was administered p.o. 20 mg/kg in the drinking water of the mice. PFST was performed on both control and montelukast-treated animals on the days 15, 30 and 60. Briefly, the mice were placed into 19 cm height 12 cm diameter glass cylinders that were filled with 25±1ºC water with a 15 cm depth for 8 minute and the immobility time of last 6 minutes was counted.

RESULTS:

In PFST, there was no significant change in the immobility at three time-points with chronic montelukast treatment compared to control group.

CONCLUSIONS:

Our results indicate that chronic montelukast treatment do not induce depression-like behavior in mice. However, neuropsychiatric side-effects of montelukast should be investigated in the presence of asthma pathophysiology.

REFERENCES:

1. Meindina G. Haarman, British Thoracic Society; Scottish Intercollegiate Guidelines Network, 2014.
2. Philip G, Hustad C, Noonan G, Malice MP, Ezekowitz A, Reiss TF et al., (2009). J Allergy and Clin. Immunol., 124(4):691-6.

OP-039: FLOATING DRUG DELIVERY SYSTEM OF ITRACONAZOLE: FORMULATION, IN VITRO AND IN VIVO STUDIES

[1] Gokbulut, E., [2] Vural, I., [3] Asikoglu M., [4] Ozdemir, N.

[1]Nobel Pharmeuticals, Ankara, Turkey

[2]Hacettepe University, Department of Pharmaceutical Technology, Ankara, Turkey

[3] Ege University, Department of Radiopharmacy, İzmir, Turkey

[4] Ankara University, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

A multiple unit oral floating drug delivery system of itraconazole (an antifungal agent) was developed to prolong gastric residence time, target stomach mucosa and increase drug bioavailability (1).

MATERIALS AND METHODS:

To prepare non-effervescent floating microspheres/ beads by ionotropic gelation method, acetic acid solution containing itraconazole and chitosan was dropped through a syringe needle into DOS or TPP (as a crosslinking agent) solution in which buoyancy is provided by swollen matrix, when the entrapped air get in touch with the gastric medium. Since the solubility of itraconazole is low at pH 1.2, it was attempted to increase the solubility by preparing inclusion complexes using RAMEB and with PVP-CL and starch. In this study, the effects of formulation parameters like concentration and types of polymer, crosslinking agent and the excipients were investigated. The floating ability, surface characteristics and drug release profiles were investigated in non-effervescent floating microspheres/beads. Since the drug release of formulation NG17 was much closer to zero order kinetics (r2=0.982), NG17 was used for cell culture studies. In Caco-2 cell culture studies, 3 different pH values (pH 5, 6 ve 7.4) were used (2).

RESULTS:

In permeability studies, with both itraconazole powder and the formulation NG17; the formulation NG17 at pH 5, which is the pH of the proximal region, showed the highest (two times of the itraconazole powder permeability) permeability value. NG17 was also used for in vivo imaging studies. NG17 was conducted in rabbits for in-vivo imaging studies by using gamma scintigraphy. It was obtained that the formulation NG17 floated for 6.5 hr in the stomach.

CONCLUSIONS:

In our study it was found that, with non-effervescent floating microsphere/bead formulations, the bioavailability of itraconazole can be improved.

REFERENCES:

1. Streubel A, Siepmann J, Bodmeier R (2006). Curr. Opin. Pharmacol., 6: 501-508.
2. Fenyvesi F, et al. (2011). J. Pharm. Sci., 100: 4734-4744.

OP-040: THE RECENT STATUS AND A PREDICTION OF THE SOCIAL PHARMACY STUDIES IN TURKEY.

Sozen Sahne, B., Ulutas Deniz, E., Yegenoglu, S.

Hacettepe University Faculty of Pharmacy, Department of Pharmacy Management and History, Ankara, Turkey

INTRODUCTION:

The social pharmacy researches are becoming more crucial with the rapid developments in pharmacy education and services (1). Pharmacy management researchers are working on the social pharmacy-related issues in Turkey in this context. It is essential to collaborate in social pharmacy studies because of its wide scope. Besides, the collaboration, which is the core of the scientific studies, is increasingly becoming important in terms of making contribution to the improvements and maintain the scientific existence (2). In this study, the current status of social pharmacy field was examined and some suggestions were made to improve its quality in Turkey.

MATERIALS AND METHODS:

Within the scope of this study, it is aimed to predict for the future of social pharmacy studies in Turkey by considering the scientific studies (articles, proceedings, books/book chapters, projects) between the years of 2013-2017 and the number of academicians who had finished or still continue their graduate education on pharmacy management.

RESULTS:

There were 15 academicians who were working in the Pharmacy Management Departments and had the above-stated qualifications in Turkey by the end of 2017. The topics of their scientific studies varied from history of pharmacy to pharmacoeconomics and ethics. According to the results of this study, the average article number per researcher was 2. Taking into account the highest and lowest article number per researchers, it's determined that this number could be increased to 6. Moreover, the lowest number of scientific studies belonged to the projects.

CONCLUSIONS:

Social pharmacy is very important for the future of the pharmacy profession in Turkey wherein the uncertainty are increasing daily for pharmacists. However, this field has its own problems like the limited number of researchers. So to contribute to the profession, this rare number of researchers should work cooperatively. Thus, it will be possible to make projects ensuring the continuity of graduate education. Creating workgroups and establishing an association will be also beneficial to increase the scientific production and visibility of the field.

REFERENCES:

1. Oltmann C, Boughey C (2012). Research in Social and Administrative Pharmacy, 8:333-337.
2. Sonnenwald DH (2007). Annual Review of Information Science and Technology, 41:643-681.

OP-041: MORPHOLOGIC REVISION OF FOUR ALLIUM L. SPECIES IN TURKEY

[1] Eksi Bona, G., [2] Koyuncu, M., [3] Duman, H., [1] Gencler Ozkan, A.M.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

[2]Cyprus International University, Faculty of Pharmacy, Department of Pharmaceutical Botany Haspolat-Lefkoşa, Cyprus

[3]Gazi University, Faculty of Science, Department of Biology, Ankara, Turkey

INTRODUCTION:

Allium L. (Amaryllidaceae) is one of the large genera of Monocotyledons, it comprises of more than 900 species in the world and approximately 200 of them grow naturally in Turkey. Allium is an important genus due to its usages as food, spice, and being ornamental plants and medicinal plants. The genus is characterized by having bulbs enclosed in membranous tunics, free or almost free tepals, and often a subgynobasic style. Most species produce remarkable amounts of cysteine sulphoxides causing the well-known characteristic odor and taste. The genus is naturally distributed only in the Northern Hemisphere, mainly in regions that are seasonally dry. It has a main center of diversity in southwest and central Asia and a second smaller one in North America (1). Allium includes some economically important species like common onion, garlic, chives, and leek under worldwide cultivation, and also species with medicinal properties. It has been investigated under 14 sections in "Flora of Turkey" (3). Sect. Cupanioscordum (1) is one of the most complicated group in Allium due to its almost similar appearances. In this study, the general morphology of the species belong to sect. Cupanioscordum has been investigated. Detailed morphological drawings, distribution maps and the descriptions are provided.

MATERIALS AND METHODS:

This study was carried out using living plants and herbarium materials belong to sect. Cupanioscordum.

RESULTS:

The diagnosis, descriptions, identification key and detailed morphological drawings are presented in detail for four Allium species distributed in Turkey.

CONCLUSIONS:

As a result, morphological characteristics of the investigated species have been expanded.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (2214-A).

REFERENCES:

1. Friesen N, Fritsch, R.M., Blattner, F.R. (2006). Aliso, 22:372–395.
2. Brullo S, Pavone P, Salmari C (2015). Flora Mediterranea, 25: 209–244.
3. Kollmann F (1984). Allium L. In: Flora of Turkey and the East Aegean Islands. Ed P.H. David. Edinburgh Univ. Press. pp 98–211.

OP-042:EVALUATION OF TURKISH OTC AND NON-PHARMACEUTICAL PRODUCTS INDUSTRY USING AN INTEGRATED SWOT AND PESTEL ANALYSIS

[1] Memisoglu, M.

[1]Biruni University, Faculty of Pharmacy, Department of Pharmacy Management, Istanbul, Turkey

INTRODUCTION:

In our previous study we conducted an interview-based qualitative analysis using in-depth, semi structured interviews of marketing professionals representing over-the counters companies as well as over-the-counter consultants in Turkey. We identified five basic themes: General Perspectives About Turkish OTC Market, Opportunities and Threats, Role of Pharmacists in Marketing Communication Process, Marketing Communication Techniques, Types of Advertising, and Internet and Social Media Usage (1). As to this study, it is a follow-up of our previous qualitative study carried out in 2015 (1).

MATERIALS AND METHODS:

In this research, by conducting a strength, weakness, opportunity, and threat analysis (SWOT), it was aimed to investigate the OTC and non-pharmaceutical products industry in Turkey. Macro-environment factors were identified by using PESTEL analysis.

Data supporting these strategic analyses were derived from multiple sources including statistical reports, literature review, and in particular our previous study.

RESULTS:

According to the results obtained, it is expected that the over the counter drugs and non-pharmaceutical products market will grow significantly. It turns out that there is a regulations requirement in this area. It has been highlighted that pharmacists who are seen as the most accessible healthcare professionals should underline their consultant identity and actively participate.

CONCLUSION:

Through conducting a thorough SWOT-PESTEL analysis, a picture of internal and external conditions of OTC and non-pharmaceutical products industry have been further clarified.

ACKNOWLEDGEMENTS:

We would like to thank all the participants who took part voluntarily in our studies and share their valuable opinions.

REFERENCES:

1. Memisoglu M (2017). Marketing communications for over-the-counter drugs and non-pharmaceutical products: the professionals' perspective. Int J Healthc Manag., 1-8.

OP-043: ESTABLISHMENT OF A DIRECT-INJECTION ELECTRON IONIZATION–MASS SPECTROMETRY METABOLOMICS METHOD AND ITS APPLICATION TO LICHEN PROFILING

[1] Kai, H., [2] Kinoshita, K., [3] Harada, H.,[4] Uesawa, Y., [1] Maeda, A., [5] Suzuki, R., [6] Okada, Y., [2] Takahashi, K., [1] Matsuno, K.

[1] Kyushu University of Health and Welfare, Department of Pharmaceutical Health Sciences, Miyazaki, Japan

[2] Meiji Pharmaceutical University, Department of Pharmacognosy and Phytochemistry, Tokyo, Japan

[3] Natural History Museum and Institute, Chiba, Chiba, Japan

[4] Meiji Pharmaceutical University, Department of Clinical Pharmaceutics, Tokyo, Japan

[5] Josai University, Department of Pharmaceutical Sciences, Saitama, Japan

[6] Meiji Pharmaceutical University, Department of Natural Medicine and Phytochemistry, Tokyo, Japan

INTRODUCTION:

Electron ionization-mass spectrometry (EI-MS) is popular due to its exceptionally wide application range with regard to sample materials. Direct-injection EI-MS (DI-EI-MS) is an ideal methodology for quality control analyses of crude drugs or other materials containing a large number of constituents. Lichens are symbiotic associations of fungi and algae found mainly in terrestrial habitats. Subtle differences in morphologic characteristics between species makes lichen identification difficult for non-taxonomists. In this study, we established a metabolomics lichen-identification method by analyzing various well-known lichen species using a combined DI-EI-MS/statistical approach.

MATERIALS AND METHODS:

Cladonia lichens were extracted with methanol at 70°C for 3 h. The extract was dried and redissolved to

5 mg/mL in dimethyl sulfoxide (DMSO). A 1-µL aliquot of test sample was injected into the DI-EI-MS system. All statistical analyses were carried out using JMP Pro 12.2 software to identify features contributing to group separation.

RESULTS:

Reproducibility of the proposed DI-EI-MS–based metabolomics method was assessed by repeated analysis of the same sample. Trough point to end of the scan in the total ion chromatogram (TIC) were integrated to account for variation in the point of maximum TIC intensity for each extract. All three reproducibility test spectra exhibited several common peaks and the same base peak at m/z 73. The established DI-EI-MS metabolomics method was then used to classify four Cladonia lichen samples. Each integrated mass spectrum exhibited characteristic peaks. For example, a peak at m/z 368 with a relative intensity of 14% was observed in the C. krempelhuberi integrated spectrum, as well as those of the other lichen extracts. All four lichen samples could be differentiated using this method. Integrated mass spectra of each extract were collected at electron energies of 70, 50, 30, and 20 eV. Minor and undistinguishable peaks were extracted for use in classification based on the absolute ion intensity at each m/z integer value. The ability to clearly distinguish four different lichen species within the same genus demonstrates the utility of the DI-EI-MS method.

CONCLUSIONS:

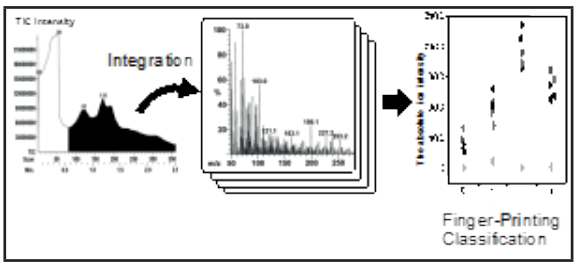
Our results suggest that metabolic profiling using DI-EI-MS is useful for discriminating between subgroups within the same species. This is the first study to report the use of DI-EI-MS in a metabolomics application.

ACKNOWLEDGEMENTS:

We thank Mr. Tadao Anzai (Zelg Co., Ltd.) for supplying C. krempelhuberi and Dr. Mitsuo Takayama (Yokohama City University) for providing EI-MS spectral data.

REFERENCES:

1. Kai H et al., (2017). Anal Chem, 89:6409-6414.
2. Kai H, et al., (2016). Lichenology, 15:117.
3. Kai H, et al., (2016). Lichenology, 14:174.
4. Suzuki R, et al., (2016). Nat Prod Commun, 11:73-75.



OP-044: DETERMINATION OF INTERGENERATIONAL CONSUMER BEHAVIOUR DIFFERENCES AMONGST GENERATIONS IN SKIN CARE PRODUCTS.

Demir, N., Yegen, G., Aksu B.

[1] Istanbul Altınbas University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Istanbul, Turkey

INTRODUCTION:

In this new time of globalization, change in science, society and strides of innovation allows individuals to have better way of life and more expectations for everyday comforts. This advancement in innovation and individual's mindfulness prompts quick development of dermocosmetic products industry, especially over the most recent ten years with the Millennial generation (1). It is a crystal-clear fact that the Millennial generation is giving more importance to their look and well-being. This brings the development of the dermocosmetic items hence this can be seen as energizer for the market (2,3). In this way, it is critical to know the effect of various factors on decision making while purchasing a dermocosmetic item (4). This can be comprehended by looking into the Millennial's dermocosmetic market and other generation's dermocosmetic market. Our study aims to search and establish purchasing habits of Millennial and other generations on dermocosmetic products and evaluate the results.

MATERIALS AND METHODS:

A Unipolar Likert Scale questionnaire was developed and distributed to Turkey consumers from different ages. A total of 100 completed questionnaire were planned to evaluate by SPSS program; upon now part of them returned and analysed manually. The sample size of 100 people includes male and female as well a working and non-working groups and also students.

RESULTS:

The aim of the study was the behaviour of different ages in Turkey with respect to dermocosmetic products. According to results of completed questionarries, for the babyboomers it's not so easy to make a purchasing decision and the quality of the product is important. Babybommers prefer to buy dermocosmetics from pharmacist and also the price is important. X generation prefer the online shopping however they also effected by friends and family members. They want to know more detail about the product that they will buy; but they are more positive than babyboomers when it comes to purchase anything. Y generation slightly know the difference between cosmetic and dermocosmetic, the product has to be trend in social media for them to buy; they don't have any preference for shopping place but online shopping more common choice.

CONCLUSIONS:

Study shows that generations have common consumption patterns, and marketing studies conducted accordingly these patterns with consideration the differences of the generations will definitely have effect the orientation of cosmetics and dermocosmetic market and the rate of sales.

REFERENCES:

1. Smith KT (2010). Journal of Strategic Marketing, 18(6):437-450.
2. Pate SS., Adams M (2013). Atlantic Marketing Journal, 2(1):7.
3. Leslie L, Bock D, Joseph M (2013). Journal of Business Strategy, 34(6):3-10.
4. Tanyel F, Stuart E, Griffin J (2013). Journal of Promotion Management, 19(5):652-673.

OP-045: STEM ANATOMY OF THE GENUS ORIGANUM L. (LABIATAE) IN TURKEY

[1] Sadikoglu, N., [2] Efe, M.

[1]Inonu University, Faculty of Pharmacy, Department of Pharmacognosy, Malatya, Turkey

[2]Mus Alparslan University, School of Health, Department of Nursing, Mus, Turkey

INTRODUCTION:

In Turkey except hybrides, 25 taxa are naturally grow in the genus *Origanum* L., commonly used as oregano (1). In particular, there are difficulties in distinguishing closely allied taxa. A detailed study has been carried out in order to distinguishing these taxa according to anatomical characteristics.

MATERIALS AND METHODS:

In this study, 24 taxa of Origanum naturally growing in Turkey, are evaluated for their stem anatomical characteristics. Cross-sections are taken from the stem at 50 microns in thickness using a microtome and photographed.

RESULTS:

It has been found that the anatomical structure of cross-sections has similarity in many directions. Stem is usually quadrangular, with the outermost layer of cuticles. Under the cuticle, 1-layered epiderma usually consisted of rectangular cells, surrounded all the stem. Below the epidermal layer there is a layer of collenchyma which varies in thickness according to the species. Under the epidermis there is a layer, thickness varies depending on the species. A discontinuous sclerenchyma layer is occur. Phloem is usually 2-8 layered variable according to the species. Pith is spread over a large area, parenchymatous, contains starch grains.

CONCLUSIONS:

In the genus Origanum, it is shown that the characteristics belong to stem of which cuticle shape, layer of epidermal cells, hair presence on epiderm, collenchyma layers both on the corners and between, layer of endodermal cells and layer of sclerenchyma are important in differentiating the taxa. All the characteristics of the stem anatomy of the genus Origanum is presented for the first time in this study.

ACKNOWLEDGEMENTS:

The authors would like to thank to Bio. İsmet GÜRHAN for photographing and preparing the materials, Fedli EKİCİ, the Director of Muş State Hospital for allowing the use of the microtome and Laboratory Assistant Murat ÇELİK for his assistance in cross-section. This study was supported by Research Fund of the Inonu University. Project Number: 2011/155.

REFERENCES

1. Sadıkoğlu N (2012). Origanum. In: Güner et al. (eds). Türkiye Bitkileri Listesi (Damarlı Bitkiler). Nezahat Gökyiğit Botanik Bahçesi ve Flora araştırmaları Derneği Yayını. İstanbul, 568-570.

OP-046: PROBING PHARMACY TECHNICIANS' SKILLS AND STATUS IN TURKEY: A FOCUS GROUP STUDY.

[1] Cavaco AM., [2] Tarhan N., [2] Arslan M., [2] Sar S.

[1] Lisbon University, Department of Social Pharmacy, Lisbon, Portugal

[2] Ankara University, Department of Pharmacy Management and History, Ankara, Turkey

INTRODUCTION:

Pharmacy technicians play important roles in the services provided in community pharmacies (1), many expanding in scope all over the world. As healthcare professionals, pharmacy technicians' work may affect directly or indirectly health outcomes (1,2). Besides technicians' roles (3), pharmacy practice research has searched the impact of education and training programs, besides professionals' certification (4,5). The aim of this study was to explore feelings, attitudes, expectations, and beliefs of pharmacy technicians regarding their duties, responsibilities and tasks, as well as educational status, therefore contributing to pharmacy practice and patient care improvement.

MATERIALS AND METHODS:

A Focus Group methodology was used to get in-depth and rich information from pharmacy technicians and pharmacists related to practice. Four focus groups were designed as follows; (i) community pharmacists only (np1=7, np2=5), (ii) pharmacy technicians only (nt1=4, nt2=7). A purposive sampling method was used to select both pharmacy

technicians and community pharmacists based on demographics heterogeneity (varying gender and age). Community pharmacists comprised those who were practicing as community pharmacy owners and had work experience with technicians as an employer. Pharmacy technicians selected were those with at least one-year of community pharmacy experience. A semi-structured interview schedule was developed to guide the moderation of the focus group discussions. Focus groups were audiotaped, transcribed verbatim and analysed thematically.

RESULTS:

Four main themes were obtained named as; professional responsibilities, daily tasks and duties, issues related to job conditions, communication features, and technicians' education. Extracted data showed pharmacists complaints on finding qualified technicians, contributing to a lack of staff that causes work problems, such as labour overload. Participants emphasized the importance of technicians' effective communication in education and training. The current technicians' education programs are found inadequate by pharmacists, being required more practice-based training.

CONCLUSIONS:

The initial evidence gathered in this study shows both community pharmacists' and technicians' feelings, attitudes and expectations about technicians' status and skills to be convergent, particularly in education and communication. Educational strategies can be re-regulated to promote technicians' qualifications, releasing pharmacists' time to more patient-centred practices.

ACKNOWLEDGEMENTS:

We want to thank pharmacists and pharmacy technicians participated in this study.

REFERENCES:

1. Rabus SA, Sancar M, Okuyan B, Izzettin F (2011). African Journal of Pharmacy and Pharmacology, 5(1):60-66.
2. Wilson DL, Kimberln CL, Brushwood, Segal R (2007). J Am Pharm Assoc., 47:588–598.
3. Kjos AL, Andreski MT (2015). J Am Pharm Assoc., 55:493–502.
4. Desselle SP (2005). J Am Pharm Assoc., 45:458–465.
5. Schmitt MR, Desselle SP (2009). J Pharm Technol., 25:79-88.

OP-047: MEDICINAL PLANTS USED FOR THE TREATMENT OF DIABETES IN ELMADAG (TURKEY)

[1] Koroglu, A., [2] Kendir, G., [1] Hurkul, M.M., [3] Koruklu, S.T., [3] Ayyildiz, G., [1] Kose, E.C.,[4] Vural, M.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Tandoğan, Ankara, Turkey

[2]İstinye University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Zeytinburnu, İstanbul, Turkey

[3]Ankara University, Faculty of Science, Department of Biology, Tandoğan, Ankara, Turkey

4Gazi University, Faculty of Science, Department of Biology, Ankara, Turkey

INTRODUCTION:

Elmadağ town is located in the northeast foothills of Elmadağ; located 41 km east of Ankara. The town which was established in the northeastern skirts of Elmadag, is a very old settlement. Elmadağ is connected to 7 neighbourhoods and 4 villages. Steppe vegetation is dominant and usually concentrated in stream beds (1, 2). The plants are used for different purposes in Elmadağ where intense urbanization is present, and they are mostly used for medicinal purposes. The aim of this study was to determine the plants used in the treatment of diabetes in Elmadağ.

MATERIALS AND METHODS:

The visits were made to the town center and villages during between 2015 to 2018. There is conducted face to face interviews with local people for collect to ethnobotanical data. The plants used by local people for diabetes in direction of the findings from interviews were determined.

RESULTS:

Due to intense urbanization in Elmadağ, much ethnobotanical information has not been obtained. In this study, it was found that more than 10 species were used in the treatment of diabetes in Elmadağ. It was observed that decoction was the most common method of preparing a herbal medicine. Findings from previous studies of Ankara towns were compared with the results obtained from this study (3, 4).

CONCLUSIONS:

When the studies of folk medicine conducted in the towns of Ankara are examined, it was determined that Astragalus sp., Prunus divaricata Ledeb., Paliurus spina-christi Mill., Berberis crataegina DC., Tribulus terrestris L. have been used against diabetes in Elmadağ, unlike these towns.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Ankara University (15A0759001).

REFERENCES:

1. Ozel A (2006). Ankara İli Elmadağ İlçesi'nin Sosyo-Ekonomik ve Kültürel Yapısı, Niğde Üniversitesi Sosyal Bilimler Enstitüsü, Niğde.
2. Terzioğlu I (2014). Elmadağ Şehrengizi, Elmadağ Belediyesinin Kuruluşunun 70. Yılı Kültür Yayını, Ankara.
3. Sarper F, Akaydın G, Simsek I, Yesilada E (2009). Turkish Journal of Biology, 33: 79-88.
4. Gunbatan T, Gurbuz, I, Gencler Ozkan AM (2016). Turkish Journal of Botany, 40: 241-249.

OP-048: THE POSSIBLE EFFECTS OF NEBIVOLOL TREATMENT ON CARDIAC CALCIUM HANDLING AND MITOGENIC ACTIVATION INDUCED BY ACUTE BETA-ADRENOCEPTOR STIMULATION.

Ozakca I, Koroglu G.

Ankara University, Faculty of Pharmacy, Department of Pharmacology, Ankara, Turkey.

INTRODUCTION:

Nebivolol is a member of third-generation β-blocker which has been approved for the treatment of hypertension. It has been known that nebivolol has cardioprotective effects including the prevention of desensitization of beta-adrenoceptor signaling and reduction of cardiac hypertrophy development (1). The aim of the present study was to investigate the possible effects of nebivolol treatment on calcium handling and mitogenic activation in the presence of acute isoprenaline stimulation in mice.

MATERIALS AND METHODS:

Twelve-week old male C57BL/6 mice were randomized into four groups (n=12): (i) Saline-injected, (ii) nebivolol-treated saline-injected, (iii) isoprenaline-injected and (iv) nebivolol-treated isoprenaline-injected. Isoprenaline was diluted in 0.9% saline and administered via intraperitoneal injection (25mg/kg). Saline control mice were injected with a calculated volume of 0.9% saline. Nebivolol hydrochloride was dissolved in drinking water (0.05g/L) for a dose of 10 mg/kg/day (1). The control group received regular drinking water. Mice were administered nebivolol for 5 days, and on day 5, they were injected with saline or isoprenaline. Mice were anesthetized by ether inhalation after 1 hour following isoprenaline injection. The heart was quickly dissected, the left ventricle tissue was immediately frozen in liquid nitrogen and stored at -80°C for western blot experiments.

RESULTS:

Nebivolol treatment significantly reduced the protein levels of phosphorylated TnI and p44/42 MAPK in controls. Phospholamban/SERCA ratio, a hallmark for evaluation of cardiac calcium handling, was not altered after 5-day nebivolol treatment. The increase in the TnI phosphorylation and Phospholamban/SERCA ratio in response to acute isoprenaline stimulation revealed the activation of cardiac beta-adrenergic signaling. Nebivolol treatment partially antagonized the acute isoprenaline-mediated calcium turnover. The increase in phosphorylation of MAPK in response to acute isoprenaline injection was not altered in the presence of nebivolol treatment.

CONCLUSIONS:

Nebivolol treatment modulates PKA-mediated signaling pathway and MAPK activation under basal conditions and in response to acute beta-adrenoceptor stimulation in different manner.

REFERENCES:

1. Ozakca I, Arioglu Inan E, Esfahani H, Altan VM, Balligand JL, Kayki Mutlu G, Ozcelikay AT (2013). Am J Physiol Heart Circ Physiol. 304:H1267-76.

OP-049: PATIENT SATISFACTION: AS A PARAMETER OF EFFECTIVE PHARMACY MANAGEMENT

[1] Sencan, NM.

[1] Acıbadem Mehmet Aydınlar University, Faculty of Pharmacy, Department of Pharmacy Management and History, Istanbul, Turkey

INTRODUCTION:

Researches done for various industries, teaches that "measuring satisfaction" is a driving force for management. Not only pharmacists' but also patient's satisfaction is a quality parameter for pharmacy and pharmaceutical services. Historically, researchers such as Donabedian, suggested measuring "patient satisfaction" as an outcome of care. This idea was expanded further by following researchers such as Ware et al., who conceptualised patient satisfaction to be a multi-dimensional construct and explained it as "an individual's assessment of clear properties of the health care" (1). As Naik Panvelkar et. Al. reasoned out that pharmacy research needs a strong measurement of patients' satisfaction in community pharmacy because of a deficiency of comprehemacists and nsive theoretical frameworks and well-designed instruments (2).

MATERIALS AND METHOD:

A patient satisfaction survey was designed as a new proprosed instrument for Turkey. Both closed and open ended questions were installed. Hard copy of 2 pages were given to patients and consumers who visited to 2 retail pharmacies in Istanbul. The reseach was conducted for 3 days.

RESULTS:

Survey itself was satisfactory practice for the patients. Nearly all the patients stated positive feedbacks both for the pharmacists and pharmaceutical services. As this is one the first researches conducted for Turkish culture, the instrument and evaluation/assesment system needed to be revised.

Conclusion: Patient satisfaction indicates consumer centered outcome. Community pharmacy services become an increasingly imperative part of the global health care system. Effects of successful implementation of pharmacy management in long-term needs to be improved and patient satisfaction measurement is a must for the evaluation.

REFERENCES:

1. Ware JE, Snyder MK, Russell W, Davies WR (1983). Evaluation and Program Planning, 6(3-4):247-263.
2. Panvelkar N, Saini B, Armour C (2009). Pharm World Sci., 31(5):525-537.

OP-050: VOLTAMMETRIC DETERMINATION OF OPHTHALMIC DRUG PROPARACAINE USING MULTI-WALLED CARBON NANOTUBE PASTE ELECTRODE

[1] Demir, E., [2] İnam, O., [3] İnam, R.

[1]Okan University, Department of Food Engineering, Faculty of Engineering, Istanbul, Turkey

[2]Hacettepe University, Faculty of Medicine, Department of Ophthalmology, Ankara, Turkey

[3]Gazi University, Department of Chemistry, Faculty of Science, Ankara, Turkey

INTRODUCTION:

Proparacaine (PPC) (2-(diethylamino)ethyl 3-amino-4-propoxybenzoate) is one of the most commonly used local anesthetic agents due to its high efficacy and fewer side effects in ophthalmic examination, minor and cataract surgeries (1). No voltammetric studies were found for the proparaine assay according to the literature review. This study is a new and sensitive method for the determination of PPC by multi-wall carbon nanotube paste electrode (MWCNTPE).

MATERIALS AND METHODS:

Voltammograms were obtained using a Bioanalytical Systems-Epsilon potentiostat/galvanostat connected to a BAS-C3 voltammetric cell stand. The MWCNTPE, Ag/AgCl (3 mol/L NaCl) and platinum wire were used as an indicator electrode, reference electrode and auxiliary electrodes, respectively.

RESULTS:

Using cyclic voltammetry, proparacaine exhibited a single irreversible anodic peak at around + 900 mV vs Ag/AgCl in pH 6.0 Britton-Robinson buffer solution. In square wave stripping voltammetry (SWSV), the deposition potential (Ed), deposition time (td), pulse amplitude (ΔE), step potential (ΔEs) and frequency (f) parameters were optimized. Proparacaine exhibited two linear sections and the dynamic linear range was found to be 0.5–12.5 mg/L with a detection limit of 0.11 mg/L. The results for the determination of proparacaine in pharmaceutical local anesthetic (Alcone®) showed that relative standard deviation (RSD) and relative error (RE) were 3.75 % and – 1.25 %, respectively. The selectivity of the method has also been examined by the recoveries of 5.0 mg/L proparacaine in the presence of 5.0 mg/L dopamine, ascorbic acid and uric acid and recoveries were 106.9 ± 0.8, 99.9 ± 1.2 and 94.1 ± 0.7, respectively.

CONCLUSIONS:

The resulting low relative standard deviation, low relative error and high recoveries showed that the reproducibility, accuracy and selectivity of the method are quite good. Thus, the voltammetric method developed for PPC is also applicable to natural samples.

REFERENCES:

1. Bartfield JM, Holmes TJ, Raccio-Robak N (1994). Academic Emergency Medicine, 1(4):364-367.

OP-051: CHEMICAL CONSTITUENTS OF PRANGOS UECHTRITZII BOISS&HAUSKN ROOTS

[1,2] Albayrak, G., [1] Demir, S., [1] Baykan, S.

[1]Ege University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Izmir, Turkey

[2]Izmir Katip Celebi University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Izmir, Turkey

INTRODUCTION:

Prangos genus., an Iran-Turan element, consisting of 17 species, is a member of Apiaceae family (1). Roots of the plant are used as aphrodisiac and wound healing agent in Anatolian folk medicine. According to previous phytochemical studies, roots of *Prangos sp.* are rich in coumarins, furanocoumarins and its derivatives. Osthol, imperatorin, oxypeucedanin, heraclenol etc. are major components of the plant (2-4). *Prangos uechtritzii* Boiss&Hauskn is a perennial herb and endemic species which is distributed in Central, East and Southeast Anatolia and the plant is known as ‘’Deli çakşır’’ (1). There are studies related to essential oil of fruits of the plant (5, 6). However, the pyhtochemistry of the plant has not been investigated previously. The aim of this study is to isolate and elucidate secondary metabolites from *P. uechtritzii*.

MATERIALS AND METHODS:

Air dried roots were extracted with chloroform using ultrasonic water bath. Fractionation and isolation studies were carried out with column chromatography and preparative TLC. Structural elucidation of the compounds was based on both spectroscopic evidence (1D, 2D NMR and MS) and reference data comparison.

RESULTS:

7 molecules have been isolated which 3 of them are coumarins and 4 are furanocoumarin derivatives. Isolated compounds were identified as suberosin, psoralen, oxypeucedanin, peucedanol, imperatorin, prantschimgin and 7-demethyl suberosin.

CONCLUSIONS:

Through our ongoing study on Prangos uechtritzii, 7 molecules have been isolated and identified so far.

ACKNOWLEDGEMENTS:

This study was supported by Katip Celebi University OYP Programme / Gökay Albayrak

REFERENCES:

1. Güner A (2012). Türkiye bitkileri listesi: (darmarlı bitkiler): ANG Vakfı
2. Tada Y, Shikishima Y, Takaishi Y, Shibata H, Higuti T, Honda G et al. (2002). Phytochemistry, 59(6):649-54.
3. Razavi SM, Nazemiyeh H, Delazar A, Hajiboland R, Rahman MM, Gibbons S et al., (2008). Phytochem Lett, 1(3):159-62.
4. Numonov S, Bobakulov K, Numonova M, Sharopov F, Setzer WN, Khalilov Q et al. (2017). Nat Prod Res, 1-8.
5. Baser KHC, Demirci B, Demirci F, Bedir E, Weyerstahl P, Marschall H et al. (2000). Planta Med, 66(7):674-7.
6. Ozcan M, Bagci Y, Akgul A, Dural H, Novak J (2000). J Essent Oil Res, 12(2):183-5.

OP-052: ANTIVIRAL, ANTINOCICEPTIVE AND ANTI-INFLAMMATORY ACTIVITIES OF THE STERILE SOLUTIONS OF ILWENSISAPONIN A AND C

[1] Diker, N.Y., [2] Kupeli, E., [3] Karaoglu, M.T., [4] Çomoglu, T., [5] Akdemir, Z.S., [1] Tatli Cankaya, I.I.

[1]Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

[2]Gazi University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

[3]Ankara University, Faculty of Veterinary Medicine, Department of Virology, Ankara, Turkey

4Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

5Hacettepe University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

The genus *Verbascum* L. (Scrophulariaceae) is represented by 228 species in the flora of Turkey (1). Infusion and decoctions of the leaves and flowers have been used for haemorrhoid, rheumatism and respiratory problems such as bronchitis, asthma and commonly used to treat wounds in traditional Turkish medicine (2, 3). Phytochemical studies of *Verbascum* species have revealed the presence of saponins, iridoids, phenylethanoids, monoterpene and neolignan glycosides, flavonoids, steroids and spermine alkaloids (4). Antiviral, antinociceptive and anti-inflammatory activities of the 1% sterile solutions of Ilwensisaponin A and C isolated from *Verbascum pterocalycinum* var. *mutense* Hub.-Mor. were assessed in this research.

MATERIALS AND METHODS:

1 % solution of the Ilwensisaponin A and C prepared by using sterile distilled water were surveyed for in vitro antiviral activity and cytotoxicity, against Rota and BHV-1 viruses. In vivo antinociceptive and anti-inflammatory activities were determined by p-benzoquinone-induced writhing and carrageenan-induced paw oedema tests in mice, respectively.

RESULTS:

According to results, antiviral activities of the 1% sterile solutions of Ilwensisaponin A and C were not mean because of cytotoxicity effect. Both solutions showed antinociceptive and anti-inflammatory activity, but solution including Ilwensisaponin A (36.8% and 9.6-36.6%, respectively) showed a high inhibition compared to Ilwensisaponin C solution (28.6% and 14.3-25.5%, respectively) for both activity methods. For anti-inflammatory activity, 1% sterile solution of Ilwensisaponin A effected phase II of acute inflammation and showed a significant inhibition compared to standard indomethacin. 1% sterile

solutions of Ilwensisaponin A and C exhibited a moderate antinociceptive activity compared to acetyl salicylic acid without gastric lesion or bleeding.

CONCLUSIONS:

1% sterile solutions of the Ilwensisaponin A isolated from V. pterocalycinum var. mutense have anti-inflammatory activity and these results are congruent with previous study (5).

REFERENCES:

1. Huber-Morath A. (1978) In: P.H. Davis (ed). Flora of Turkey and The East Aegean Islands, Vol. 6. University Press, Edinburgh, pp 461.
2. Baytop T (1999), Therapy with Medicinal Plants in Turkey (Past and Present), 2nd ed. Nobel Tıp Kitabevleri Ltd., Istanbul, pp 334.
3. Sezik et al., (2001). Journal of Ethnopharmacology, 75: 95-115.
4. Tatli II and Akdemir ZS (2004). FABAD Journal of Pharmaceutical Sciences, 29: 93-107.
5. Kupeli et al., (2007). Journal of Ethnopharmacology, 110: 444-450.

OP-053: PROTECTIVE EFFECT OF MTOR INHIBITION ON LPS-INDUCED SYSTEMIC INFLAMMATION AND TISSUE INJURY: CONTRIBUTION OF MTOR/IKB-A/NF-KB/ HIF-1A SIGNALING PATHWAY AND NADPH OXIDASE SYSTEM ACTIVITY

Guden, DS., Temiz Resitoglu, M., Kucukkavruk, SP., Tunctan, B., Sahan Firat, S.

Mersin University, Department of Pharmacology, Mersin, Turkey

INTRODUCTION:

Recently, it has become clear that the hypoxia-inducible transcription factor (HIF) pathway plays a key role in the regulation of immunity and inflammation (1). However, the relationship between nuclear factor (NF)-κB and HIF-1α is proved elusive (2,3). Rapamycin (RAPA) is a potent immunosupressant agent that effects cell cycle, growth, autophagy, and protein synthesis through mammalian target of rapamycin (mTOR) activity (4). As a continuation of our previous studies, we hypothesized that mTOR inhibition may prevent LPS-induced hypotension, inflammation and oxidative stress via modulation of mTOR/IκB-α/NF-κB/HIF-1α signaling pathway.

MATERIALS AND METHODS:

Male Wistar rats received saline (4 ml/kg, i.p.), LPS (10 mg/kg, i.p.) and/or RAPA (1 mg/kg, i.p.) at time 0. Mean arterial pressure (MAP) and heart rate (HR) were measured by using a tail-cuff device. Rats were sacrificed 4 h after LPS challenge. Blood, kidney, heart, and lung were harvested for the measurement of expression and/or phosphorylation of rpS6, IκB-α, NF-κB p65, HIF-1α, iNOS, TNF-α, IL-1β, gp91phox, p47 phox, and β-actin, also nitrite levels in tissues and/or sera.

RESULTS:

MAP decreased and HR increased in the LPS administered rats. LPS caused an increase in expression and/or phosphorylation of rpS6, IκB-α, NF-κB p65 and HIF-1α, TNF-α, IL-1β, iNOS and oxidative stress markers (gp91phox and p47 phox), a decrease in IκB-α expression with increased nitrite levels in tissues and/or sera. These changes caused by LPS were prevented by RAPA, the selective mTOR inhibitor. RAPA alone had no effect on the parameters measured.

CONCLUSIONS:

These findings suggest that mTOR activation enhances the expression of proinflammatory mediators and contributes to the development of tissue injury by inducing stimulation of IκB-α/NF-κB/HIF-1α signaling pathway and NADPH oxidase system activity.

ACKNOWLEDGMENTS

This work was supported by the grant from the Research Foundation of Mersin University (BAP-2017-1-TP3-1995).

REFERENCES:

1. Palazon A et al., (2014). Immunity, 41:518–528.
2. Scholz CC, Taylor CT (2013). Current Opinion in Pharmacology, 13:646-653.
3. Rius J et al., (2008). Nature, 453:807–811.
4. Liu YC et al., (2017). Neuroscience, 355:188-199.

OP-054: DESIGN OF OXYGEN-RICH ELECTRODE PLATFORMS FOR ENZYMATIC SENSING

Uzunoglu, A.

Necmettin Erbakan University, Metallurgical and Materials Engineering, Konya, Turkey

INTRODUCTION:

Oxidase enzymes have been widely used as biological elements in electrochemical biosensors for both lactate and glucose detections. Although oxidase enzymes pose many advantages including high sensitivity and selectivity towards the corresponding analytes, they suffer from oxygen dependency. Since oxidase enzymes use oxygen as an electron accepter (mediator) in enzyme reactions, any fluctuation in dissolved oxygen concentration in environments results in false readings. In addition, it is noteworthy that the dissolved oxygen concentration in human blood fluctuates significantly depending on the health conditions. In the present work, we designed novel

electrode surfaces by exploiting oxygen-rich surfaces of CeO_2 and CeO_2-based nanoparticles to eliminate the oxygen dependency challenge.

MATERIALS AND METHODS:

The nanoparticles were synthesized by a facile co-precipitation method and characterized by SEM, TEM, XRD, XPS, Raman, and TGA methods. The biosensors were constructed by drop casting certain amount of nanoparticle and enzyme solutions on polished glassy carbon electrode surface. Amperometry and cyclic voltammetry techniques were employed to evaluate the performance of the biosensors.

RESULTS:

It was observed that the oxygen release property of the nanoparticles had a profound impact on the performance of the biosensors in O2-depleted environments. While unmodified biosensors experienced a significant decrease in their response in oxygen-lean medium, the modification of enzyme layer with CeO2-based nanoparticles declined the O2-susceptibility of the sensors significantly.

CONCLUSIONS:

False readings and errors in biosensor responses were minimized by the modification of enzyme layer with O2-rich materials.

OP-055: IN VITRO ANTIMICROBIAL AND ANTIBIOFILM EFFECTS OF THYMOL AGAINST CLINICAL METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS ISOLATES

[1] Ates, A., [1] Temel, A., [2] Kayin, M., [2] Tunger, A., [1] Ermertcan, S.

[1]Ege University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Izmir, Turkey

[2]Ege University, Faculty of Medicine, Department of Medical Microbiology, Izmir, Turkey

INTRODUCTION:

Methicillin-resistant Staphylococcus aureus (MRSA) is a multidrug resistant bacteria and one of the most prominent bacterial pathogens which causes medical device associated infections by biofilm formation (1,2). Bacteria are can be more resistant to antibiotics in the biofilm layer (3). The increase of antibiotic resistance increased interest in studying the antimicrobial potency of phytochemicals.In this study, we investigated antimicrobial and antibiofilm efficacy of thymol which is a phenolic monoterpene, on MRSA strains.

MATERIALS AND METHODS:

Twenty MRSA strains isolated from clinical samples at Ege University, Faculty of Medicine, Bacteriology Laboratory of Medical Microbiology Department. Identification and the antimicrobial susceptibility profiles of isolates was performed using VITEK 2 system. Minimum inhibitory concentrations (MIC) of thymol were determined by broth microdilution method according to EUCAST criteria. The biofilm production of isolates and anti-biofilm effects of thymol were investigated by spectrophotometric microplate method.

RESULTS:

The MIC values of thymol was detected 64 µg/ml in one isolate and was 256 µg/ml in nineteen isolates. Sixteen isolates and four isolates were identified as moderate and strong biofilm producers, respectively. It was determined that biofilm formation was decreased in twelve isolates and increased in one isolates, by addition of sub-MIC/2 of thymol. The effects of sub-MIC of thymol on mature biofilm formation in isolates are shown in Table 1.

Table 1. Effect of thymol on mature biofilm in moderate and strong biofilm producers

	Effects on mature biofilm	Thymol MIC/2	Thymol MIC/4
Number of isolates(n)	Decrease	12	14
	Increase	1	1
	Stable	7	5

CONCLUSIONS:

In this study, we have demonstrated that thymol which is a major phenolic component of oregano oil, may have inhibitory effects on mature biofilm structure and may help to prevent MRSA-associated biofilm infections.

REFERENCES:

1. El-Azizi M, Rao S et al. (2005). Annals of Clinical Microbiology and Antimicrobials, 4:2.
2. Diep BA, Otto M (2008). Trends In Microbiology, 16(8):361–369.
3. Bendouah Z, Barbeau J et al. (2006). Otolaryngology-Head And Neck Surgery, 134(6):991–996.

OP-056: ELECTROCHEMICAL DETECTION OF NASAL DECONGESTANT DRUG OXYMETAZOLINE BY -COOH FUNCTIONALIZED MWCNTS AND TITANIA NANOPARTICLES MODIFIED ELECTRODE

[1] Munir, A., [2] Bozal Palabiyik, B., [1] Shah, A., [2] Uslu, B.

[1]Quaid-i-Azam University, Department of Chemistry, Islamabad, Pakistan

[2]Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Oxymetazoline, a nasal vasoconstrictor drug, has been used as nasal decongestant for more than forty years (1). No electrochemical study has previously been performed on oxymetazoline to illustrate the electrochemical fate of this drug. Moreover, not any modification of electrodes has been reported in the literature for this drug. However, the present study was conducted in order to bridge this gap and to get useful insights about the fabrication of electrode and redox mechanism of oxymetazoline.

MATERIALS AND METHODS:

-COOH functionalized multi-walled carbon nanotubes (MWCNTs) and TiO2 nanoparticles (NPs) were used for the modification of glassy carbon electrode (GCE). Differential pulse voltammetry and cyclic voltammetry was employed for the illustration of electrochemical redox mechanism. While, electrochemical impedance spectroscopy and differential pulse voltammetry was used for the determination of performance of sensor developed.

RESULTS:

The results revealed enhanced electrochemical behavior of oxymetazoline by TiO2NPs/fMWCNTs/GCE as compared to bare GCE. The conditions were optimized at pH 7.0 phosphate buffer solution, 0 V accumulation potential, and 180 s accumulation time. The differential pulse voltammetric response of oxymetazoline was determined between the linear concentration range of 0.05 µM to 1.5 µM. In pH 7.0 phosphate buffer solution, oxymetazoline gave three anodic peaks in the studied potential range. The possible redox mechanism was proposed for all the three peaks. While, only two of these peaks were studied for the determination of oxymetazoline with the limit of detection values of 4.40 nM and 9.84 nM for both peaks.

CONCLUSIONS:

The nanomolar concentration of oxymetazoline drug was successfully determined by the current developed method. The possible electron transfer mechanism of this novel drug was suggested effectively. The validation of present technique was assessed and the amount of oxymetazoline in pharmaceutical nasal spray was successfully determined.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (2216)

REFERENCES:

1. Mahajan MK, Uttamsingh V, Daniels JS, Gan LS, LeDuc BW, Williams DA (2011). Drug Metabolism and Disposition, 39:693–702.

OP-057: APPLICATION, CHARACTERIZATION AND COMPARATIVE ANTIMICROBIAL ACTIVITY OF HYPERICUM AUCHERI JAUB. & SPACH VE HYPERICUM PERFORATUM L. EXTRACTS CONJUGATED HYBRID NANOFLOWERS

[1] Ildiz, N., [2] Baldemir, A., [1] Ince, U., [2] Ilgun, S., [3] Ocsoy, I.

[1]Erciyes University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Kayseri, Turkey

[2]Erciyes University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Kayseri, Turkey

[3]Erciyes University, Faculty of Pharmacy, Department of Analytical Chemistry, Kayseri, Turkey

INTRODUCTION:

Hypericum L. genus (Hypericaceae) are represented a hundered species in Turkey (1). In this study, the upper parts of the flowering soil of Hypericum perforatum (Balikesir-Edremit) and H. aucheri species were collected from Balıkesir-Kazdağları Sarıkız hill and diagnosed (ERCH 5112, 5113).

MATERIALS AND METHODS:

Methanol extracts of the plants were prepared from the underground parts of H. perforatum and H. aucheri by maceration method. The total phenol contains of the extracts were calculated using the Folin-Ciocalteu method as the gallic acid equivalent. The scavenging activity of DPPH radicals of the extracts were also studied. In addition, for the first time the synthesis, characterization and antimicrobial activities of extract+Cu2+ hybrid nanoflowers (NFs) from both methanol extracts were investigated according to CLSI) standards at 7,825 – 500 µg/ml concentrations. Synthesized nanoflower structures were identified by SEM, EDX and FTIR.

RESULTS:

According to the results, H. aucheri species is richer in phenolic content than H. perforatum. The antimicrobial activity about four times higher than H. perforatum on other tested microorganisms (Staphylococcus aureus ATCC 29213, Bacillus subtilis ATCC 6633, Acinetobacter baumanni ATCC 19606, Pseudomonas aeruginosa ATCC 27853, Candida albicans ATCC 90028) than Escherichia coli ATCC 35218 and Enterococcus faecium ATCC 8459 in their

antimicrobial activity experiments. Also antimicrobial effect of hypericin was tested. There were no effect of hypericin and hypericin NF on tested microorganisms. NFs were two fold more effective on tested microorganisms than extracts at low concentrations (7,825 µg/ml) against especially Gram negatives. In addition, A. baumannii and P.aeruginosa, which have high resistance to treatment, appear to have high antimicrobial activity at low dose (62.5 µg/ml). Both extracts were evaluated for DPPH radical scavenging effects as percent inhibition and were equally effective when compared to the standard materials used.

CONCLUSIONS:

As a result, H. aucheri species may be a candidate plant species for which standardization studies can be performed when comparing activity and content with H. perforatum. Interestingly, nanoflowers that synthesized from plant extracts have promising with high stability and antimicrobial effect.

REFERENCES:

1.Baytop T (1983). Therapy with Medicinal Plants in Turkey. Istanbul University Press, Istanbul, pp 197.

OP-058: NOSE TO BRAIN DELIVERY OF ELETRIPTAN HYDROBROMIDE PLGA NANOPARTICLES

Esim O., Savaser A., Ozkan CK., Tas C., Ozkan Y.

University of Health Sciences, Department of Pharmaceutical Technology, Etlik, 060[1]8 Ankara, Turkey

INTRODUCTION:

The objective of this study was to prepare Eletriptan Hydrobromide loaded PLGA nanoparticles and provide brain targeting, and sustained release of Eletriptan Hydrobromide with-in the brain. This benefit would help to improve its clinical utility in migraine, reduce side effects and improve therapeutic efficacy.

MATERIALS AND METHODS:

PLGA nanoparticles (NP) were prepared using the W/O/W emulsion technique. Release of Eletriptan Hydrobromide from the nanoparticles was studied at 37°C using a dialysis bag diffusion technique. The released drug in the buffer was collected at predetermined time intervals and frozen for further quantitative analysis using HPLC (1). To investigate the cytotoxicity of Eletriptan Hydrobromide with or without encapsulation into PLGA, CaCo2 cells. The intracellular Eletriptan Hydrobromide accumulation was examined as described (2). Nanoparticulate formulation and drug solution were administered intranasal (IN) or intravenously (IV). Subsequently, rats were sacrificed at different time intervals and their brains were removed and homogenized in PBS (pH 7.4).

RESULTS:

Nanoparticles were prepared with a particle size 244.3±28.1 nm and 0.110± 0.05 PDI. More than 80 % of drug was released after 24 h and cell viability of Eletriptan Hydrobromide with encapsulation into PLGA in CaCo2 cells were higher than free drug. The highest brain drug concentration was observed after intranasal nanoparticle administration.

CONCLUSIONS:

It can be concluded from study that it is possible to prepare Eletriptan Hydrobromide−PLGA nanoparticles. PLGA NP showed no significant toxicity on CaCo2 cells, Drug efflux studies showed that PLGA nanoparticles can inhibit the function of P-gp and increase. From the results of in vivo studies, one can conclude that the NP provided a higher brain concentration of drug after IN administration compared with IN- and IV-administered drug solution. Thus, it can be concluded that drug-loaded PLGA NP are capable of providing direct nose-to-brain delivery, thereby enhancing drug concentration in the brain.

ACKNOWLEDGEMENTS:

This study was supported by a grant of University of Health Sciences (2017/006)

REFERENCES:

1. Esim, O et al. (2017) Journal of Pharmaceutical and Biomedical Analysis 142: 74-8.
2. Seju, U., A. Kumar, and K. K. Sawant. (2011) Acta biomaterialia 7.12 4169-4176.

OP-059: ESTIMATION AND PREPARATION OF DRY POWDER INHALER FORMULATIONS THAT CONSISTING OF CIPROFLOXACIN HCL LOADED NANO AND MICROCOMPOSITE PARTICLES FOR PULMONARY ADMINISTRATION

[1] Topal, GR., [1] Devrim, B., [2] Eryilmaz, M., [1] Bozkir, A.

[1] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

[2] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Ankara, Turkey

INTRODUCTION:

Pulmonary delivery of antibiotics has many advantages for treatment of lung infections comparing to others. Inhalation of drugs may lead to much higher drug concentrations in pulmonary tissue (1). However, drugs of conventional inhalation therapy results in a short duration of drug action at the target site. Therefore, there is a need to design of sustained release formulations to localize the drug action in the lungs (2, 3). The most important advantage of nanoparticles is their small size and ability to cross

various barriers, increase the contact surface with the tissue. However high cohesive properties due to the large surface area is a problem in the preparation. Preparation of low-density microparticles provide controlling of nanoparticle sizes and surface charges, and agglomerates. They are called nanocomposite microparticles, they will be easily separated into nanoparticles in aqueous media in the lungs and aerosolized. In this study, ciprofloxacin(CIP)-loaded nanoparticles and nanocomposite microparticles for pulmonary delivery were developed and evaluated in-vitro. The nanoparticles were prepared in order to encapsulate the hydrophilic CIP. Nanocomposite microparticles were prepared using nanoparticle to obtain micron size required for pulmonary delivery.

MATERIALS AND METHODS:

CIP was gift from Zentiva-Turkey. Dichloromethane, poly-€-caprolactone (PCL), PLGA-50/50 (MA=40000-75000/MA=24000-38000), polyvinyl alcohol (Mw=30000–70000) were obtained from Sigma (Germany). Chitosan-HCl was purchased from NovaMatrix (Norway). CIP-loaded nanoparticles were prepared by solid-in-oil-in-water emulsion-solvent evaporation method and the effects of various formulation parameters on the physicochemical properties of the nanoparticles were investigated. Composite microparticles were prepared using mannitol as a carrier and aerodynamic proporties were investigated. Antibacterial activity test was carried out with agar diffusion method employing the cup plate technique (4).

RESULTS:

PCL-nanoparticles showed spherical shapes with particle sizes around 143-489nm. Encapsulation efficiency was found to be low because of water-solubility properties of CIP. CIP-loaded PCL-nanoparticles showed initial burst effect for 4h and continuously released for 72h. Tapped density and MMADt results showed nanocomposite microparticles have suitable aerodynamic properties for pulmonary administration. Antimicrobial activity test indicated CIP-encapsulated PCL-nanoparticles and nanocomposite microparticles inhibited growth of bacteria.

CONCLUSIONS:

Surface modification of nanoparticles with chitosan caused an increase in encapsulation efficiency. Antibacterial activity test indicated, ciprofloxacin retained its antimicrobial efficacy when incorporated in the particular system. Considering nanoparticles 0 and 6th month activities, the particular system was stabile. As a result, nanocomposite microparticles containing CIP-loaded nanoparticles can be used for pulmonary delivery.

REFERENCES:

1. Zhang J. et al. 2011. Advanced Drug Delivery Reviews, 63:441-455.
2. Yhee JY, Im J., Nho R.S. 2016. Journal of Clinical Medicine, 5: 82.
3. Elhissi A, 2017. Current Pharmaceutical Design, 23(3), 362-372.
4. Moazeni E et al. 2010. Journal of Microencapsulation, 27(7):618-627.

OP-060: INVESTIGATION OF PERFLUOROALKYL SUBSTANCES IN TAP WATER SAMPLES TAKEN FROM SEVERAL PROVINCES IN TURKEY

[1] Unlu Endirlik, B., [1] Bakir, E., [1] Bosgelmez, II.,[1] Eken, A., [2] Narin, I., [3] Gurbay, A.

[1]Erciyes University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Kayseri, Turkey

[2]Erciyes University, Faculty of Pharmacy, Department of Analytical Chemistry, Kayseri, Turkey

[3]Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Ankara, Turkey

INTRODUCTION:

Perfluorinated compounds, which are widely used in many industrial and consumer products for over 60 years, bioaccumulate in the environment due to their high persistence. Several human and animal studies have shown an association between exposure to these compounds and adverse health effects on many organs and systems (1). The most common exposure pathway for humans to perfluorinated compounds are considered to be contaminated drinking water and foods (2). In the literature, levels of perfluoroalkyl substances (PFASs) were investigated in ground, surface, tap or bottled water in various countries (3) and, to our knowledge, present study is the first research performed in Turkey.

MATERIALS AND METHODS:

Forty-nine samples of tap water were collected from 33 provinces of Turkey. The samples were extracted by solid phase extraction and analyzed via ultra performance liquid chromatography-tandem mass spectrometry for the presence of 10 different PFASs: PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFBS, PFHxS and PFOS.

RESULTS:

Method detection limit was calculated separately for each PFAS and ranged between 0.07 and 0.12 ng/L. Highest concentrations of PFOA, PFOS, PFHxA, and PFBA in tap water samples was determined as 1.37, 1.25, 1.82 and 1.69 ng/L, respectively, while other PFASs were also detected in considerable levels. In general, tap water samples from İstanbul, Eskişehir, İzmir and Ankara were found to have highest PFAS levels.

CONCLUSIONS:

The results show that PFAS levels tend to be higher in urbanized and industrialized places. Since this is the first investigation measuring tap water PFAS levels in different locations in Turkey, additional studies with other water sources (groundwater, surface waters, wastewater, etc.) should be performed to confirm our results.

ACKNOWLEDGEMENTS:

This study was supported by Research Fund of the Erciyes University (TSA-2017-7144).

REFERENCES:

1. Lindstrom AB, Strynar MJ, et al., (2011). Polyfluorinated compounds: past, present, and future. Environmental Science & Technology, 45(19):7954-7961.
2. Domingo JL (2012). Health risks of dietary exposure to perfluorinated compounds. Environment International, 40:187-195.
3. Llorca M, Farré M, et al., (2012). Analysis of perfluoroalkyl substances in waters from Germany and Spain. Science of the Total Environment, 431:139-150.

OP-061: DETERMINATION OF ANTI-INFLAMMATORY AND ANTIDIABETIC ACTIVITIES OF 14 BALLOTA TAXA GROWING IN TURKEY

[1] Yazgan, A.N., [2] Yilmaz Sarialtin, S., [3] Can Agca, A., [2] Coban, T., [1] Saltan Iscan, G., [1] Sever Yilmaz, B.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Ankara, Turkey

[3]Turkish Medicines and Medical Devices Agency, Ankara, Turkey

INTRODUCTION:

Ballota species belong to Lamiaceae family commonly distributed in the mild climate locations and have been used in folk medicine as antiulcer, antispasmodic, antihemorrhoidal and sedative agents (1). Inflammation is a protective mechanism in response to an abnormal stimulation caused by a physical, chemical, or biological agent. Some non-steroidal drugs and corticosteroids currently used for inflammatory conditions have toxic effects (2, 3). Diabetes mellitus is a major endocrine disorder and is characterized by abnormalities in carbohydrate, lipid and lipoprotein metabolisms (4). Plants secondary metabolites have extensively different bioactivity properties. The aim of this study was to examine 14 *Ballota* taxa from Turkey for their antidiabetic and anti-inflammatory activities.

MATERIALS AND METHODS:

In this study aqueous and alcoholic extracts of 14 *Ballota* taxa were examined for their antidiabetic and anti-inflammatory activities by using in vitro α-glucosidase inhibitory activity and membrane stabilization method, respectively (3, 5).

RESULTS:

Aqueous extract of B. nigra subsp. anatolica exhibited the maximum anti-inflammatory effect following by ethanolic extracts of B. acetabulosa and B. glandulosissima. And for antidiabetic activity, aqueous and ethanol extracts of B. glandulosissima (IC50=2.18 and 2.30 µg/ml respectively) exhibited the maximum α-glucosidase inhibitory activity.

CONCLUSIONS:

The ethanolic extracts showed higher membrane stabilization profile than aqueous extracts generally. In contrast, the aqueous extracts showed higher α-glucosidase inhibitory activity than the ethanol extracts. It is concluded that the solvent type could affect the profile of biologically active components.

ACKNOWLEDGEMENTS:

There is no acknowledgement to be declared in this study.

REFERENCES:

1. Citoglu G, Tanker M, Sever B, Englert J, Anton R, Altanlar N (1998). Planta Medica, 64: 484-485.
2. Dinarello CA (2010). Cell, 140: 935-950.
3. Singh R, Patil SM, Pal G, Ahmad M (2012). Asian Pacific Journal of Tropical Disease, 2: 404-407.
4. Ozkan G, Kamiloglu S, Ozdal T, Boyacioglu D, Capanoglu E (2016). Molecules, 21: 1-32.
5. Liu X, Zhu L, Tan J, Zhou X, Xiao L, Yang X, Wang B (2014). BMC Complementary and Alternative Medicine, 14: 1-10.

OP-062: DEVELOPMENT AND EVALUATION OF ETOPOSIDE LOADED POLYMERIC TUBULAR NANOSTRUCTURES

Algan, AH, Karatas, A.

Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Besides nanocarrier size, shape of the nanocarrier is a critical parameter which has an impact on circulation time (1). Studies have shown that cylindrical nanostructures, circulate longer than spherical particles with the same diameter (2). Template synthesis is one of promising ways of fabrication of tubular nanostructures (3). Etoposide (ETP) is a chemotherapeutic agent with poor aqueous solubility and short half-life (4). The aim of the study was to produce ETP loaded polymeric tubular nanostructures by template wetting of nanoporous membranes.

MATERIALS AND METHODS:

Anodic aluminum oxide(AAO) (Whatman™, GE Healthcare) was template membrane. Poly-ε-caprolactone(PCL), Poly-d,l-lactide-co-glycolide(PLGA), poly(l-lacticacid-co-caprolactone-co-glycolic acid) (PLCG) were purchased from Sigma-Aldrich.

Preparation of etoposide loaded polymeric tubular nanostructures

Polymer and ETP were dissolved in a mixture of dichloromethane (DCM) and dimethyl formamide (DMF). For wetting AAO membrane template, immersion technique was applied in ETP/polymer solution for a predetermined time in tightly close glass containers. Drug/polymer embedded AAO membranes were dried at room temperature in order to remove all residual solvent. AAO template etching was performed with aqueous phosphoric acid to dissolve AAO completely. After etching of the template membranes, liberated tubular nanostructures were collected by vacuum filtration, washed with pure water, and they were freeze dried.

RESULTS:

ETP assay was conducted by HPLC analysis which was described in our previous work (5). Entrapment efficiency (EE%) and drug loading (DL%) were calculated.

Table1. Evaluation of formulations

Code	Polymers	Solvent system	Polymer / ETP ratio	EE (%)	DL (%)
F1	PCL	DCM:DMF	10:2	10.25	1.71
F2	PLGA	DCM:DMF	10:2	18.21	3.04
F3	P(LCG)	DCM:DMF	10:2	12.08	2.01

The morphology of the polymeric tubular nanostructures were examined by scanning electron microscopy(SEM). Images showed that ETP loaded nanostructures were obtained successfully in nano dimensions and with smooth surfaced tubular forms.

CONCLUSIONS:

Consequently, the developed polymeric tubular nanostructures was found promising and improvable for the delivery of antineoplastic agents.

ACKNOWLEDGEMENTS:

This work was supported by the Scientific and Technological Research Council of Turkey (TUBITAK) under Grant 113S201.

REFERENCES:

1. Maeda H, Wu J, Sawa T, Matsumura Y, Hori K (2000). J. Control. Release, 65 (1-2): 271-28.
2. Champion JA, Katare YK, Mitragotri S (2007). J. Control. Release, 121 (1-2): 3-9.
3. Son SJ, Bai X, Nan A, Ghandehari H, Lee SB. (2006) J. Control. Release, 114:143-152.
4. Najar IA, Johri RK (2014). J. Biosci., 39 (1):139-144.
5. Algan AH, Gumustas M, Karatas A, Ozkan SA (2016). J Pharm Biomed Analysis, 124: 382-389.

OP-063: PREPARATION AND IN VITRO CHARACTERIZATION OF DEXAMETHASONE LOADED ETHOSOME FORMULATIONS

Rencber, S., Tuncay Tanriverdi, S.

Ege University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Izmir, Turkey

INTRODUCTION:

The purpose of this study was to prepare and characterized ethosomal formulation containing Dexamethasone (DEX) for topical application.

METHODS:

Ethosomal formulations were prepared according to the method reported by Tanrıverdi et. al., 2013. Phospholipid and DEX were dissolved in ethanol. Distilled water was added slowly to the lipid mixture with constant stirring. The resulting vesicle suspension was homogenized with using probe sonicator. The formulations were prepared with two different ratio of phospholipid. The zeta potential (ZP), particle size (PS) and polydispersity (PI) were determined by light scattering spectroscopy. The pH values of the formulations were determined by using a pH meter. For encapsulation efficiency (EE), ethosomal formulations were ultracentrifuged, the supernatant was used for DEX analysis by validated HPLC method and the quantity of free drug was determined. The drug loading (DL) and amount of drug were

determined by dissolving the ethosome suspensions in methanol. Morphological analysis was performed by transmission electron microscopy. The dialysis bag diffusion technique was used to study the in vitro drug release. 1 mL of ethosome suspensions was placed in the dialysis bag, hermetically sealed and immersed into pH 5.5 sorenson buffer. Samples were withdrawn from the receptor compartment at predetermined time intervals. The amount of drug released was determined by HPLC. The dissolution data were fit to Peppas equation, and best-fit parameters were calculated to determine the release mechanism of formulations.

RESULTS:

Ethosomal formulations were successfully prepared using modified ethanol injection method. The pH values of the F1 and F2 formulations were found to be 7.68 and 7.53, respectively. Neutral pH values indicated the formulation could be used as topical delivery with low risk skin irritation. PS, PI and ZP of the formulations were given in Table 1.The EE% of DEX from the ethosomal formulations was as high as 84.119%–77.254%. The amount of drug was found 95.099 and 95.133%, respectively. Also, DL capacity was found 5.039% and 8.648%, respectively. Figure 1 shows that prepared all formulations controlled drug release. According to Peppas equation, the values of n fell within the range of 0.671-0.756, indicating that the drug release from the NPs is non-Fickian.

CONCLUSION:

The objective of the present work of formulation and evaluating of DEX ethosomal formulations for topical delivery has been achieved with success.

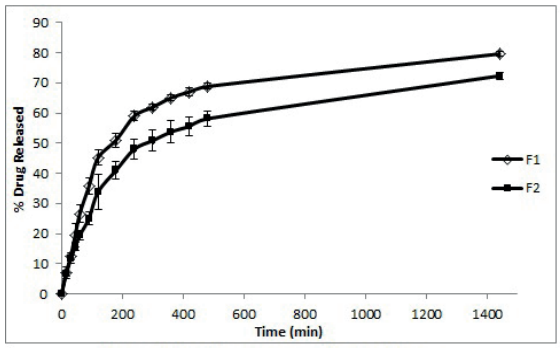


Figure 1. *In vitro* release of formulations

Table 1. PS, PI and ZP of formulations

Formulation Code	PS (nm)±SD	PI±SD	ZP (mV)±SD
F1	997.40±2.75	0.290±0.033	0.532±0.06
F2	930.28±2.37	0.443±0.011	0.695±0.09

OP-064: HIGH PERFORMANCE LIQUID CHROMATOGRAPHY ANALYSIS OF SECONDARY METABOLITES FROM VAGINAL LACTOBACILLUS SPECIES

[1] Gurpinar, S.S., [1] Eryilmaz, M., [2] Palabiyik, I.M.,[3] Gerceker, D.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Ankara, Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

[3]Ankara University, Faculty of Medicine, Department of Medical Microbiology, Ankara, Turkey

INTRODUCTION:

Inefficiency in treating the infections caused by multi-resistance microorganisms have brought about the necessity for new compounds with antimicrobial activity. The genus Lactobacillus has recently been focal point of researchers due to their ability to produce secondary metabolites with antimicrobial effects such as lactic acid, acetic acid and hydrogen peroxide (1). The aim of this study was to determine the quantities of lactic acid, acetic acid and hydrogen peroxide in secondary metabolites from vaginal Lactobacillus species by High Performance Liquid Chromatography (HPLC).

MATERIALS AND METHODS:

Vaginal isolates were identified through 16S rRNA method. Lactobacillus isolates were inoculated into tubes containing De Man-Rogosa Sharpe Broth at 37 ºC, under anaerobic conditions for 72 hours. After incubation, cells were removed by centrifugation (12000 g, 10 min, 4 °C). Cell free supernatants were filter-sterilized (2). HPLC analysis of secondary metabolites were carried out on Agilent 1100 series. Separation was carried out on Inertsil ODS-3 (150 length x 4.6 mm i.d., 5 µm). Elution was performed with a mobile phase as % 0.025 phosphoric acid solution. The flow rate was set at 0.75 mL/min, injection volume was 5 µL and temperature of the column was maintained at 25ºC. Compounds were detected at a wavelength of 210 nm.

RESULTS:

In this study, of the 53 vaginal isolates identified through 16S rRNA method, 18 were established to be L. crispatus, 17 L. gasseri, 5 L. jensenii, 4 L. vaginalis, 3 L. fermentum, 2 L. coleohominis, 1 L. saerimneri, 1 L. reuteri, 1 L. johnsonii and 1 L. helveticus species. According to the HPLC analysis results, secondary metabolites of all tested isolates contain hydrogen peroxide between 0,007306 and 0,00033 mg/µL range. It was found that the secondary metabolites of some isolates contained both acetic and lactic acid, while some of them contained either acetic or lactic acid at various concentrations.

CONCLUSIONS:

Lactobacillus species are different from each other in terms of secondary metabolites production quantities. Lactic acid, acetic acid and hydrogen peroxide may be responsible for their antimicrobial activity. Based on this difference, the antimicrobial activity of these species may change.

ACKNOWLEDGEMENTS:

This study was supported by Ankara University Scientific Research Council (17H0237011).

REFERENCES:

1. Pithva S, Ambalam P, Dave JM, Vyas BRM (2011). Formatex, 987-991.
2. Stoyancheva G, Marzotto M, Dellaglio F, Torriani S (2014). Arch Microbiol, 196:645–653.

OP-065: ASSESSMENT OF PERFLUOROOCTANOIC ACID TOXICITY MECHANISMS IN PANCREATIC CELLS

[1] Abudayyak, M., [2] Oztas, E., [2] Baran, T., [2] Ozhan, G.

[1]Karadeniz Technical University Department of Pharmaceutical Toxicology, Trabzon, Turkey

[2] Istanbul University, Department of Pharmaceutical Toxicology, Istanbul, Turkey

INTRODUCTION:

Perfluorooctanoic acid (PFOA) has been widely used in the industrial field since 1950's, and detected in surface waters, house dusts, and in human blood serum due to direct or indirect exposure during production, uses and disposal. PFOA, considered to be endocrine disrupting and teratogenic agent, has been investigated as a cause of cardiovascular disease, peripheral arterial disease, immunological system impairment and liver damage. In 2017, PFOA was classified by the International Cancer Research Agency (IARC) as a possible carcinogen for humans (group 2B). The in vivo studies have reported that PFOA might lead to hepatic, testicular and pancreatic cancers. However, the mechanism in pancreatic tissues is still unclear and insufficiently discussed. Inflammation effects are the most important mechanisms leading to pancreatitis and afterwards cancer. Activation of trypsinogen is one of the important biomarkers in acute pancreatitis and other pancreatic injuries (1,2). In this study, it has been aimed to investigate whether inflammation effect is one of the PFOA-induced cancer mechanisms in the pancreatic tissue

MATERIALS AND METHODS:

The cytotoxic activity was measured by MTT assay, the apoptotic effect was evaluated using annexin V/PI, caspase-3/7 and by Bax levels. The chymotrypsin, trypsin, IL-6, IL-8, MAPκ-8, TNFβ and TNFα inflammation related enzyme and cytokine levels were measured using flow cytometry, RT-PCR, and spectrophotometry. The oxidative stress MDA, GSH, CAT and SOD levels were evaluated by ELISA kits, and the ROS level was measured using flow cytometry.

RESULTS:

Our results show that PFOA caused a cell death in concentration dependent manner (IC50 195.6 μM), and apoptosis might not be the major cell death pathway. A significant increase in chymotrypsin but not in trypsin levels were detected in the exposed cells. The significant change in some oxidative stress end points and inflammation related proteins/gene levels indicated the role of oxidative damage and inflammation in PFOA induced toxicity.

CONCLUSIONS:

Inflammation and oxidative stress play an important role in PFOA induced toxicity. Further studies should be conducted to better understand how effect the inflammation mechanisms-induced ROS in the toxicity of PFOA.

REFERENCES:

1. Ma Z, et al., (2016). Oncotarget, 7(41), 66558–66568.
2. Negri E, et al., (2017). Critical Reviews in Toxicology, 47(6), 489–515.

OP-066: GREEN SYNTHESIS OF SILVER NANOPARTICLES FROM THE EXTRACT OF MOLLUGO CERVIANA (L.) SER. FOR ANTIMICROBIAL APPLICATIONS

[1] Napagoda, M., [1] De Soyza, S., [2] Wijayaratne, G., [3] Witharana, S.

[1] University of Ruhuna, Faculty of Medicine, Department of Biochemistry,Galle, Sri Lanka

[2] University of Ruhuna, Faculty of Medicine, Department of Microbiology, Galle, Sri Lanka

[3]Faculty of Engineering, Higher Colleges of Technology, United Arab Emirates

INTRODUCTION:

Silver has a long empirical history of human usage in medicine to treat and prevent microbial infections. Silver is found to be even more effective in antimicrobial activity when the particles are at nanoscale. The conventional physio-chemical approaches in the synthesis of silver nanoparticles involve expensive and often hazardous chemical agents. Therefore, the development of cost-effective and greener methods to synthesize silver nanoparticles has become a research highlight in recent times [1]. Present study was undertaken to synthesize silver nanoparticles using methanol extract of Mollugo cerviana (L.) Ser. and to evaluate its antimicrobial and disinfectant properties subsequently.

MATERIALS AND METHODS:

Methanolic extract prepared from the seeds of M. cerviana (L.) Ser. was tested against Gram positive and Gram negative bacteria by disc diffusion and broth micro-dilution methods. Thereafter, the extract was treated with silver nitrate. The subsequent development of silver nanoparticles was observed using UV-visible spectrophotometer and scanning electron microscopy. The antibacterial and antifungal activity of the resulted nanopreparation was evaluated thereafter.

RESULTS:

Despite the wide utility of this plant as an antimicrobial medication, the original plant extract was not capable of inhibiting the growth of the tested bacteria even at a high concentration of 1000 µg/mL. Nevertheless, when the silver nanopreparation was obtained from this extract, a noticeable activity was observed. The change in the original colour of the reaction mixture and the increased UV-Visible absorbance indicated that phytochemicals present in the extract could reduce silver ions into elemental silver. The size and morphology of the synthesized nanoparticles were revealed by scanning electron microscopy as clusters in the vicinity of 100 nm. Although the antifungal activity of this nanopreparation against Candida albicans was negligible, the antibacterial potential was conspicuous against Staphylococcus aureus, Enterococcus faecalis and methicillin-resistant S. aureus with minimum inhibitory concentration values in the range of 125-250 µg/mL.

CONCLUSIONS:

The use of natural plant extracts such as methanolic extract of M. cerviana (L.) Ser. in the preparation of silver nanoparticles by a greener route would provide advancement over conventional methods due to the cost effective and eco-friendly features. The preliminary results of this study suggest that the synthesized silver nanoparticles has a high potential to be developed into a novel disinfectant. Thus, the experiments are in progress to confirm its' disinfectant potential, mechanism of action and also to exclude the possible cytotoxic effects on human.

ACKNOWLEDGEMENTS:

This study was supported by SLMA-Glaxo Welcome Research grant-2017

REFERENCES:

1. Makarov et al., (2014). Acta Nature 6(20):35-44.

OP-067: METABOLITE CHANGES OF PROTEUS MIRABILIS IN POLY-SPECIES BIOFILM MODELS

[1] Kart, D, [2] Nemutlu, E.

[1]Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Ankara, Turkey

[2]Hacettepe University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Proteus mirabilis is one of the major agents in a variety of hospital acquired infections and also isolated from the biofilm related infections. Differantial dynamic relations and interactions have been found in mixed-species biofilms by comparison with their single-species biofilms. P. mirabilis, E. faecalis and C. albicans are frequently grow together and isolated from the samples of infected patients. Our goal was to establish an poly-species biofilm model in vitro and to find out the impact of presence of the C. albicans and E. faecalis on metabolite profile of P. mirabilis.

MATERIALS AND METHODS:

Proteus mirabilis ATCC 29906, Enterococcus faecalis ATCC 47077 and Candida albicans SC5314 were used in the study. Polymicrobial biofilms were reproducibly grown, consisting of C. albicans, E. faecalis and P. mirabilis in a 96-well microtiter plate. Comparative metabolomic analysis of mono and polymicrobial biofilm samples was carried out based on the GC-MS metabolomic profiling to scan wide range of metabolites. Distribution of metabolites was analysed by the Kyoto Encyclopedia of Genes and Genomes metabolic pathways database.

RESULTS:

The number of P. mirabilis biofilm cells was found significantly higher in dual and triple species biofilms than single-species. The multivariate metabolomic analysis shows clear separation between mono and polymicrobial biofilm groups of E. faecalis (Figure 1). After deconvolution and aligned of the chromatograms, 189 mass spectral features have been detected and 118 of them were annotated using retention index libraries. Aminoacyl-tRNA synthesis, D-glutamine and D-glutamate, glutathione, alanine, aspartate and glutamate and nitrogen metabolisms significantly changed in multi-species biofilms compared to single-species biofilm by the pathway analysis method.

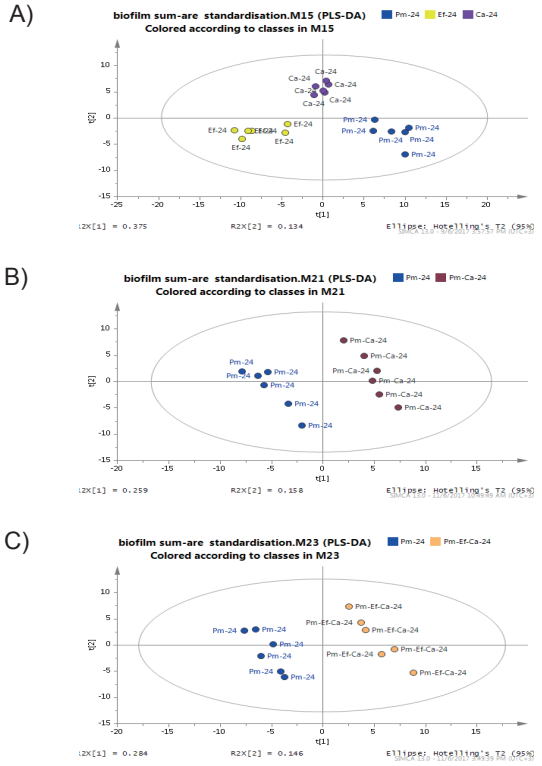


Figure 1:The metabolomic profile of P.mirabilis in mono, dual and triple species biofilms.

CONCLUSIONS:

E. faecalis and P. mirabilis association in dual and triple biofilm resulted in increased amino acid and pipecolic acid synthesis intermediates when compared to only E. faecalis biofilm, displaying a rerouting of metabolic pathways.

OP-068: ANTIMICROBIAL SUSCEPTIBILITY OF ESCHERICHIA COLI ISOLATED FROM VARIOUS CLINICAL SAMPLES

[1] Kayan, S., [1] Gurpinar, S.S., [1] Eryilmaz, M., [2] Vuran, S., [2] Gerceker, D.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Ankara, Turkey

[2]Ankara University, Faculty of Medicine, Department of Medical Microbiology, Ankara, Turkey

INTRODUCTION:

Increased resistance to antimicrobials is a major problem in the treatment of infections caused by resistant microorganisms in worldwide. *Escherichia coli* is a Gram-negative, rod-shaped bacterium that is one of the most frequent cause of many common bacterial infections, including bacteremia, cholecystitis, cholangitis, urinary tract infection, and traveler's diarrhea, and other clinical infections such as neonatal meningitis and pneumonia (1, 2). This study was conducted to determine the antimicrobial susceptibility patterns of 80 *Escherichia coli* strains isolated from various clinical samples.

MATERIALS AND METHODS:

A total of 80 E. coli isolates (59 urine, 9 sputum, 4 blood, 3 tissue, 2 drain, 2 vagina, 1 peritoneum) were obtained from Ankara University, Faculty of Medicine, Cebeci Hospital Central Laboratory. Isolates were identified both by the conventional methods and MALDI-TOF MS. Antimicrobial susceptibility testing was conducted on Mueller-Hinton Agar plates (Merck, Germany) using disc diffusion method in accordance with EUCAST (The European Committee on Antimicrobial Susceptibility Testing) recommendations. Results were expressed as susceptible or resistant according to the criteria recommended by EUCAST (3, 4).

RESULTS:

The resistance rates detected were 42.5 % to amoxicillin clavulanic acid, 36.25 % to cefotaxime, 32.5 % to ceftazidime, 7.5 % to gentamicin, 1.25 % to amikacin, 42.5 % to cephalothin, 3.75 % to imipenem, 8.75 % to ertapenem, 47.5 % to ciprofloxacin, 46.25 % to levofloxacin, 57.5 % to trimethoprim/sulphamethoxazole, 1.25 % to nitrofurantoin, 11.25 % to piperacillin/tazobactam, 13.75 % to cefoxitin, 33.75 % to fosfomycin, 32.5 % to cefepime and 71.25 % to ampicillin.

CONCLUSIONS:

When the high resistance rates are taken into consideration, antibiotic usage policies and empirical therapies should be based on antimicrobial resistance surveillance studies.

REFERENCES:

1. Tham J (2012). Extended-Spectrum Beta-Lactamase-Producing Enterobacteriaceae: Epidemiology, Risk Factors, and Duration of Carriage (Vol. 2012, No. 65). Department of Clinical Sciences, Lund University.
2. Centers for Disease Control and Prevention (CDC).*Escherichia coli*, (https://www.cdc.gov/ecoli/)
3. EUCAST Disk Diffusion Method for Antimicrobial Susceptibility Testing - Version 6.0 (January 2017).
4. The European Committee on Antimicrobial Susceptibility Testing. Breakpoint Tables for İnterpretation of MICs and Zone Diameters. Version 7.1, Valid from 2017-03-10.

OP-069: ESTROGEN RECEPTOR MODULATING EFFECTS OF ST. JOHN'S WORT

[1] Tascioglu, A., [1] Uslu, D., [1] Toker, Y., [2] Bedir, E., [1] Gurer Orhan, H.

[1] *Ege University, Faculty of Pharmacy, Department of Toxicology, Izmir, Turkey*

[2] *IZTECH, Faculty of Bioengeneering, Izmir, Turkey*

INTRODUCTION:

Exposure to phytoestrogens is associated with the increased risk of hormone-related breast cancer in postmenopausal women (1). St John's Wort (SJW-*Hypericum* sp.) is a dietary supplement that is commonly used in the treatment of depression in postmenopausal women. The present study is undertaken to evaluate estrogen receptor (ER) modulatory effects of SJW and its biflavonoid constituents, biapigenin and amentoflavone.

MATERIALS AND METHODS:

SJW extracts were prepared by ethanol:distilled water:DMSO (70:25:5) extraction. The biflavonoids of SJW were isolated with LC and identified by ESI-MS, NMR and ESI-TOFMS analysis. Estrogenic activities of SJW extract, amentoflavone and biapigenin were investigated by in vitro fluorescence based ER-binding and cell proliferation-based E-Screen assays. In vivo uterotrophic assay was also performed as the gold standard estrogenicity assay.

RESULTS:

Biflavonoid constituents of SJW were separeted with HPLC and identified in NMR analysis. Binding affinity of SJW to ER was detected as IC50:2,2 mg/ml. Although SJW extract has proliferative effect on MCF-7/BUS cells (EC50:0,0124 mg/ml), its biflavonoids didn't induce proliferation of cells. In vivo uterotrophic assay didn't confirm the estrogenic effect of the extract.

CONCLUSIONS:

SJW extract is found to cause proliferation of ER(+) breast cancer cells probably by binding of its component(s) to the ER. On the other hand amentoflavone and biapigenin, did not cause proliferation in MCF-7/BUS cells and did not bind to the ER. Furthermore neither SJW extract nor biapigenin administration to Wistar rats altered the uterus weight in in vivo uterotrophic assay at physiologically relevant concentrations. As a conclusion, SJW etract seem to have an estrogenic effect and some of its secondary metabolites, other than biflavonoids, should be responsible for this action. However this effect seems not to be relevant physiologically with the consumption of dietary supplements.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (108S202) and Ege University Research Fund (11ECZ003 and 11ECZ007).

REFERENCES:

1. Diamanti Kandarakis, E, et al., (2009). Endocrine-disrupting chemicals: an Endocrine Society scientific statement. Endocrine reviews, 30(4):293-342.

OP-070: ANTIOXIDANT ACTIVITY, HPTLC FINGERPRINT AND DISCRIMINANT ANALYSIS OF PLANTAGO MAJOR LEAVES FROM DIVERSE ORIGINS IN INDONESIA

Kartini, K.

University of Surabaya, Department of Pharmaceutical Biology, Surabaya, Indonesia

INTRODUCTION:

Plantago major L. (Plantaginaceae) is a perennial herb having contribution to the folk medicine all around the world [1], including Indonesia with wide geographical distribution [2]. Plant materials origin is one factor that significantly influences the quality of herbal medicines.

MATERIALS AND METHODS:

In this paper, HPTLC method using pattern-oriented approach has been employed to evaluate the quality of Plantago major leaves collected from seven origins in Indonesia. To differentiate the antioxidant capacities of those plant materials, the crude extracts were tested using DPPH, total phenolics, and total flavonoids assay methods.

RESULTS:

The results showed that radical scavenging activity, total phenolics, and total flavonoids of plant material from seven origins were significantly different. Moreover, HPTLC fingerprints analyzed with chemometrics showed an ability to discriminate the leaves samples from various origins. Two models using principal component analysis (PCA) and partial least squares (PLS-DA) were built in chemometrics test. The PCA model was able to describe the studied samples by using four principal components with a value of explained variance of 95%, whereas PLS-DA model accurately classified the leaves samples with prediction ability of 100%.

CONCLUSIONS:

Plantago major collected from different origins revealed different radical scavenging activity and concentration of total phenolics as well as total flavonoids. HPTLC fingerprints analyzed with chemometrics can be used as an alternative of marker-oriented method to evaluate the quality of Plantago major.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Republic of Indonesia (contract number 373.11/E4.4/K/2012).

REFERENCES:

1. Samuelsen AB (2000). Journal of Ethnopharmacology, 71(1-2):1-21.
2. Kartini, Piyaviriyakul S, Siripong P, Vallisuta O (2014). Industrial Crops and Products, 60:239-246.

OP-071: PYOCYANIN PRODUCTION OF PSEUDOMONAS AERUGINOSA ISOLATES AND DETERMINATION OF ANTIMICROBIAL ACTIVITY

Erol, H.B., Yildiz, S.

Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Ankara, Turkey

INTRODUCTION:

Pseudomonas aeruginosa is Gram-negative bacterium found in almost every ecological niche as soil, water and plants. It is often isolated from the contaminant regions and may produce metabolites (ie, rhamnolipid, pyocyanin) that enhance its competitiveness and survival (1). Pyocyanin is the characteristic blue-green phenazine pigment produced by P. aeruginosa. The presence of P. aeruginosa and the production of pyocyanin may alter the microbial community structure by inhibiting the growth of microorganisms sensitive to pyocyanin (2). The optimization of pyocyanin production was carried out in the different conditions of cultivation. The objectives of this study were: [1] to isolate different P. aeruginosa strains from soil sample; [2] to enhance pyocyanin production of isolates [3] and study the functional activity of pyocyanin against standart strains.

MATERIALS AND METHODS:

Thirty-one soil sample were collected from different region in Ankara. Four P. aeruginosa isolates [A-D] producing the finest pigments were selected for this study. For comparison; four different synthetic artificial media [1-4] were used for P. aeruginosa proliferation and pigment production. These media are listed in Table 1. Pyocyanin production were carried out according to Priyaja method and weight of the dried pyocyanin was determined gravimetrically (3).

Table 1: Comparison of media for pyocyanin production (mg/L) by 4 strains of Pseudomonas aeruginosa in 72 hours at 37 °C.

Media*	Strain A	Strain B	Strain C	Strain D
1	2,86	0,93	3,33	1,2
2	0,73	0,8	1,2	0,46
3	0,33	0,33	0,26	0,33
4	0,86	0,93	0,93	0,53

* Mediums with different contents.

The assay of antibacterial and antifungal of pyocyanin was carried out in agar well diffusion and disc diffusion method (4). Escherichia coli ATCC 25922, Escherichia coli ATCC 35218, Staphylococcus aureus ATCC 25923, Staphylococcus aureus ATCC 43300, Staphylococcus epidermidis ATCC 12228, Klebsiella pneumoniae ATCC 13883 and Candida albicans ATCC 10231 standard strains were used in this study.

RESULTS:

The production of pyocyanin can be improved by culture 1 ve 2. The present study has demonstrated that pyocyanin production by all isolates had antimicrobial activity against Gram-positive bacteria more than Gram negative bacteria and the yeast.

CONCLUSIONS:

As a result, production of the pyocyanin has been found to depend on the media content and properties of the isolates. Pyocyanin produced in different media showed various antibacterial and antifungal activity spectrum.

REFERENCES:

1. Onbasli D, Aslim B (2008). African Journal of Biotechnology, 7:4614-4619.
2. Norman RS, Moeller P, McDonald TJ, Morris PJ (2004). Applied and Environmental Microbiology, 70:4004-4011.
3. Priyaja P, Jayesh P, Rosamma P, Bright Singh IS (2016). Cytotechnology, 68:143-155.
4. Torino MI, Taranto MP, Sesma F, Font de Valdez G (2001). Journal of Applied Microbiology, 91:846-852.

OP-072: STUDIES ON MICROORGANISMS TO BE USED IN EFFICACY TESTS FOR ANTIMICROBIAL AGENTS

Kiymaci, M.E., Yildiz, S.

Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Ankara, Turkey

INTRODUCTION:

The methods applied to test the efficacy of antimicrobial agents used to interfere with antimicrobial functions differ depending on the nature of the agents. In some of these standard test methods like “The Society of Industrial Technology for Antimicrobial Articles or ASTM E.2149 methods” etc., spesific microorganisms

are suggested for testing the antimicrobial activity of antimicrobial agents under dynamic contact conditions, but it is mentioned that some of Gram positive or negative microorganisms may be used as standards too. In this study, we aimed to investigate the usability of eleven microorganisms in one of these standard test methods.

MATERIALS AND METHODS:

The antibacterial performance test method for antibacterial products specified in Term 2 of JIS Z28015 was used (1). Staphylococcus aureus ATCC 6538, Staphylococcus aureus ATCC 25923, Staphylococcus aureus ATCC 29213, Staphylococcus aureus ATCC 43300, Staphylococcus epidermidis ATCC 35984, Staphylococcus epidermidis ATCC 12228, Escherichia coli ATCC 25922, Escherichia coli ATCC 35218, Klebsiella pneumoniae ATCC 13883, Klebsiella pneumoniae RSKK 574 and Pseudomonas aeruginosa ATCC 27853 were tested as microorganisms.

RESULTS:

The results of the tested microorganisms at the 0th and 24th h were shown in the Table 1. and Table 2. as cfu/mL.

Table 1. Growth results of tested Gram (+) bacteria at 0^{th} and 24^{th} hour as cfu/mL.

Test Hour	Test Microorganisms					
	S.aureus ATCC 6538	*S.aureus* ATCC 25923	*S.aureus* ATCC 29213	*S.aureus* ATCC 43300	S.epidermidis ATCC 35984	S.epidermidis ATCC 12228
0^{th} h	$8.4x10^3$	$6.9x10^3$	$4.8x10^3$	$9.6x10^3$	$3.3x10^3$	$5.7x10^3$
24^{th} h	$4.06x10^4$	$3.0x10^2$	$4.7x10^4$	$3.0x10^6$	$1.5x10^3$	$1.0x10^3$

Table 2. Growth results of tested Gram (-) bacteria at 0th and 24th hour as cfu/mL.

Test Hour	Test Microorganisms				
	E.coli ATCC 25922	*E.coli* ATCC 35218	*K.pneumoniae* ATCC 13883	*K.pneumoniae* RSKK 574	*P.aeruginosa* ATCC 27853
0^{th} h	$4.4x10^3$	$9.6x10^3$	$7.0x10^2$	$2.7x10^3$	$7.9x10^3$
24^{th} h	$2.8x10^6$	$3.0x10^6$	$4.7x10^7$	$3.4x10^5$	$3.0x10^6$

CONCLUSIONS:

A standard test method based on determining the antibacterial activity performance of antibacterial agents was investigated. In this method, 1/500 diluted nutrient broth (with sterile distilled water, pH 7.0) was used for production of microorganisms and this medium was not provide a convenient environment for each microorganism. It was determined that the use of S. aureus ATCC 25923, S. epidermidis ATCC 35984 and S. epidermidis ATCC 12228 was not appropriate in “The Society of Industrial Technology for Antimicrobial Articles: Test Method II” shake flask method due to their 24 h growth results. On the other hand all Gram negative microorganisms were found to be suitable for this test method.

REFERENCES:

1. The Society of Industrial Technology for Antimicrobial Articles: Test Method II, Shake Flask method, the antibacterial performance test method for antibacterial products. JIS Z28015 (2012). Link: http://www.kohkin.net/dcms_media/other/S06-e.pdf.

OP-073: EFFECT OF ANTICOAGULANTS ON ETHINYL ESTRADIOL AND LEVONORGESTREL ANALYSIS IN PLASMA USING LIQUID CHROMATOGRAPHY TANDEM MASS SPECTROMETRY

[1] Yahdiana, H., [1] Devina, [1] Firda Zakiatun, N., [2] Sunarsih

[1]Indonesia University, Faculty of Pharmacy, Kampus UI Depok, Depok, Indonesia

[2]Deamedika Clinic, Indonesia

INTRODUCTION:

There are many kinds of anticoagulants often used to obtain plasma from whole blood. The most commonly used anticoagulants are ethylenediamintetraacetic acid (EDTA), heparin, and citrate. Different types of anticoagulants may cause suppression or enhancement ionization efficiency of analytes or metabolites. This research investigated the effect of the various anticoagulants on the recovery, peak area, stability, and matrix effects of ethynil estradiol and levonorgestrel analysis in plasma using LC-MS/MS (1,2).

MATERIALS AND METHODS:

Analysis was performed on Waters Xevo TQD using positive electrospray ionization with Acquity UPLC BEH Waters C18 (2,1 × 100 mm; 1,7 µm) column; mobile phase consisted of 0.1% (v/v) formic acid in water and acetonitrile in gradient elution; flow rate of 0.3 ml/min; and prednisone as internal standard. Analyte extraction from human plasma was conducted using a combination of liquid-liquid extraction (LLE) and solid phase extraction (SPE). Detection of the mass was performed for ethinyl estradiol, levonorgestrel and prednisone with m/z value: 530.1596 > 171.0781; 313.1596 > 245.1044; 359.0957 > 147.0364, respectively.

RESULTS:

This method was linear in the concentration range of 5-500 pg/ml for ethinyl estradiol and 100-1000 pg/ml for levonorgestrel with r value > 0,999. Comparisons of some parameter analysis indicated that there were no statistically significant differences ($p > 0,05$; ANOVA) in citrate, heparin, and EDTA of ethinyl estradiol and levonorgestrel analysis in human plasma for recovery and stability. On the other hand, peak area response ratio for the three plasma showed a significant difference ($p < 0,05$).

CONCLUSIONS:

There was no statistically significant differences in citrate, heparin, and EDTA plasma in recovery and stability, but for peak area response ratio for the three plasma showed a significant difference.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Directorate of Research and Community Services Universitas Indonesia, Indonesia

REFERENCES:

1. Barri T, Dragsted LO (2013). Analytica Chimica Acta, 768(1), 118–128.
2. Wheaton J, Chambers E, Fountain K (2012). Bioanalysis, 4(7), 769-781.

OP-074: POLY(2-ETHYL-2-OXAZOLINE) AS AN ALTERNATIVE TO POLY(VINYLPYRROLIDONE) IN SOLID DISPERSIONS FOR SOLUBILITY AND DISSOLUTION RATE ENHANCEMENT OF DRUGS

[1] Fael, H., [2] Ràfols, C., [1] Demirel, AL.

[1] Koc University, Department of Chemistry, Istanbul, Turkey

[2] Universitat de Barcelona, Departament de Química Analítica, Barcelona, Spain

INTRODUCTION:

Amorphous solid dispersions effectively enhance solubility, dissolution rate and thus, the bioavailability of poorly soluble drugs. Solid dispersion consists mostly of a hydrophilic polymer and a hydrophobic drug (1). Poly(2-ethyl-2-oxazoline) (PEOX), a biocompatible polymer and a pseudo polypeptide, has recently received significant attention for its biomedical applications (2). While poly(vinylpyrrolidone) (PVP) is a commonly used polymer for solid dispersion preparation, PEOX has not been used before for this purpose. The different dynamic and conformational properties of PEOX and PVP chains in aqueous solution are expected to have a potential impact on PEOX ability to stabilize the saturated solution induced after the dissolution of amorphous drugs by inhibiting the crystal nucleation and the crystal growth of the drug molecules (3). This work reports the first investigation of PEOX solid dispersion with a BCS class II model drug, glipizide (GPZ), introducing PEOX as an alternative to PVP for the preparation of solid dispersions.

MATERIALS AND METHODS:

GPZ-polymer solid dispersions were prepared by solvent evaporation and characterized by PXRD, DSC, SEM, and FTIR. The impact of polymers on crystal nucleation kinetics was investigated. Solubility and dissolution behavior of the prepared solid dispersions were in-vitro evaluated at different pH values and in fasted simulated intestinal fluid (FaSSIF).

RESULTS:

PEOX exhibited strong crystal nucleation inhibitory effect compared to PVP. A significant enhancement in glipizide solubility was obtained with PEOX compared to the pure drug and solid dispersion with PVP. A big improvement in the intrinsic dissolution rate (45 times) and dissolved amount of glipizide was achieved with PEOX in FaSSIF.

CONCLUSIONS:

The findings of this study with glipizide as a model drug introduce PEOX as a good alternative to PVP and promising polymeric carrier toward better oral bioavailability of poorly soluble drugs.

ACKNOWLEDGEMENTS:

This study was supported by Koc University and IIE-SRF.

REFERENCES:

1. Chiou et al., (1971). Journal of pharmaceutical sciences, 60:1281-1302.
2. Mero et al., (2008). Journal of Controlled Release, 125:87-95.
3. Ilevbare et al., (2012). Crystal Growth & Design, 12:3133-3143.

OP-075: A NEW LC METHOD FOR QUANTITATIVE ESTIMATION OF AVANAFIL IN COMBINATION TABLETS

[1,2] Levent, S., [2,3] Ozcan, S., [2,3] Can, NO.

[1]Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskisehir, Turkey

[2]Anadolu University, Faculty of Pharmacy, Doping and Narcotic Compounds Analysis Laboratory, Eskisehir, Turkey

[3]Anadolu University, Department of Analytical Chemistry, Faculty of Pharmacy, Eskisehir, Turkey

INTRODUCTION:

Avanafil (AVA), a pyrimidine–derivative phosphodiesterase-5 inhibitor, is one of the most effective drugs prescribed for erectile dysfunction (1). In the current work, a new LC method, in which MS/MS or photodiode array detector (PDA) can be utilized, was developed for determination of AVA in dapoxetine (DPX)/AVA combination tablets.

MATERIALS AND METHODS:

The separation of AVA and DPX was carried out using a second generation C18-bonded monolithic silica column (Chromolith® High Resolution RP-18e, 100×4.6 mm, Merck KGaA) as stationary phase, and a solution consisted of 0.1% (v/v) formic acid in water and 0.1% (v/v) formic acid in acetonitrile (75: 25 (v/v), pH=2.6) as mobile phase. The flow rate was 0.5 mL/min, and the column temperature was maintained at 40.0 °C. Sample injection volume was 1 µL for LC-PDA and 0.3 µL for LC–MS/MS analyses. The method was validated according to ICH Q2(R1); moreover,

the specificity and robustness of the method, as well as stability of AVA solutions were studied.

RESULTS:

The limit of quantitation (LOQ) and limit of detection (LOD) were found to be 3.55 ng/mL and 1.17 ng/mL for MS/MS detection; LOQ and LOD were 0.217 µg/mL and 0.072 µg/mL, for PDA respectively. The developed method allowed quantitative determination of AVA in combination tablets with high accuracy (%95.43 for LC-PDA; %102.09 for LC-MS/MS) and precision (0.229 %RSD for LC-PDA and 0.401 %RSD for LC-MS/MS).

CONCLUSIONS:

The method proposed in this study has a high level of flexibility due to use of very similar chromatographic conditions for MS/MS and PDA detection, and also reliable and easily applicable. Any analyst can select one of the two detection techniques and related injection volume, according to the instrumental facilities of the laboratory.

ACKNOWLEDGEMENTS:

Authors would like to acknowledge Anadolu University Scientific Research Projects Commission for financial and technical support (Project No: 1606S567).

REFERENCES:

1. Kedia GT, Uckert S, Pour AF, Kuczyk MA, Albrecht K (2013). Therapeutic Advances In Urology, 5(1): 35-41.
2. ICH Harmonised Tripartite Guideline: Validation of Analytical Procedure Text and Methodology Q2 (R1), International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, 2005.

OP-076: DEVELOPMENT AND VALIDATION OF AN HPLC METHOD FOR AMLODIPINE BESYLATE AND ENALAPRIL MALEATE USING AN EXPERIMENTAL DESIGN AND ITS APPLICATION TO SOLUBILITY AND DISSOLUTION TESTS

[1] Sarisaltik Yasin, D., [2] Arslanturk Bingul A., [3] Karakucuk, A., [3] Teksin ZS.

[1]Dicle University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Diyarbakir, Turkey

[2]Dicle University, Faculty of Pharmacy, Department of Chemistry, Diyarbakir, Turkey

[3]Gazi University, Faculty of Pharmacy, Department of. Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

The aim of this study was to develop a simple, rapid and robust HPLC method for the determination and separation of AB and EM according to design of experiment (DoE) for development of fixed dose tablet combinations. The solubility of APIs and dissolution studies of commercial products (Norvasc® and Enalap®) were also performed using the optimized method.

MATERIALS AND METHODS:

The validation of the method was carried out according to ICH guidelines (1) using HPLC (Shimadzu LC-20A, photodiode array detector) with RP-C18 column (5 µm, 250x4.6 mm, Waters) at 215 nm. Box-Benkhen design was used to test robustness of the method (Design Expert® Version 9.0). Flow rate (1, 1.2, and 1.4 mL/min), column temperature (20, 25, and 30 oC), methanol ratio (5, 10, and 15%), and pH of the mobile phase (2.8, 3, and 3.2) were selected as independent variables. 29 experiments were performed. Concentrations and retention times of AB and EM were evaluated. Shake flask method (2) was used for solubility of drugs. Solubility was conducted at pH 1.2 in 37˚C (n=3). Dissolution was performed using USP apparatus II at pH 1.2 (n=3)

RESULTS:

Two-way interactions between independent variables were found insignificant ($p>0.05$). Linear models were used for all variables. The optimized method was selected as following parameters: 25oC of column temperature, 10.6% methanol, pH 2.95 and 1.205 mL/min of flow rate. Retention times were 3.79 min and 7.93 min for EM and AB, respectively. Linearity was shown with coefficient of correlation (r2) of 0.999. Solubility values were found 27.1 ± 2.7 mg/mL and 2.68 ± 0.1 mg/mL for EM and AB, respectively. Both AB and EM were dissolved more than 85% in 10 min.

CONCLUSIONS:

DoE was found useful tool for developing analytical method validation of AB and EM. The optimized method can be used for in vitro performance and quality control tests of fixed dose tablet combinations containing AB and EM.

REFERENCES:

1. International Conference on Harmonization (ICH) Q2(R1) (1995).
2. Glomme A et al., (2005). Journal of Pharmaceutical Science, 94(1),1-16.

OP-077: DETERMINATION OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS IN HUMAN MILK BY DLLME-HPLC

Alsoul, S., Hassan, M., Alshana, U.

Near East University, Department of Analytical Chemistry, Faculty of Pharmacy, Nicosia, TRNC, Mersin

INTRODUCTION:

Since the discovery of dispersive liquid-liquid microextraction (DLLME) in 2006 by Assadi Y. (1), it gained a pronounced reputation among other techniques due to its simplicity, cost-effectiveness, rapidity and low organic solvent consumption while providing excellent sample clean-up and high preconcentration factors. In this study, DLLME with back-extraction was used prior to HPLC for the extraction and determination of four nonsteroidal anti-inflammatory drugs (NSAIDs) [i.e., ketoprofen (KET), etodolac (ET), flurbiprofen (FBP) and ibuprofen (IBU)] in human milk.

MATERIALS AND METHODS:

The analytes were separated using a 1200 SERIES Agilent Technologies Gradient HPLC with a Diode-Array Detector (DAD), a reversed-phase column (i.e., Grom-Sil 80 Octyl-4 FE, 4.6 mm ID 250 mm, 3 µm), a mobile phase consisting of ACN:1.0% TFA, 40:60 (%, v/v) at pH* 1.4, flow rate 0.8 mL min-1, temperature 40 °C and injection volume of 20 µL.

RESULTS:

The analytes were extracted from milk (2.0 mL) into ACN (4.0 mL) by salting-out extraction, 2.5 mL of which then were used as the disperser solvent in DLLME. Other optimum DLLME conditions were achieved using 200 µL chloroform (extraction solvent), aqueous solution completed to 11 mL with 3% (w/v) NaCl and extraction time of 1 min. Back-extraction of NSAIDs into 100 µL of ACN:1.0 M NaOH, 30:70 (%v/v) solution within 1 min resulted in enrichment factors of 7.2 to 10.0 and limits of detection (LOD) as low as 0.20 mg L-1. Coefficients of determination (2) of the calibration graphs were higher than 0.9951. Three different human milk samples with breastfeeding age of 2, 6 and 12 months from three healthy volunteers were studied and showed minimum matrix effect on the extraction efficiency of the proposed method. Finally, DLLME-HPLC was applied to determine FBP in genuine milk samples at different time intervals (0.5-3.5 h) after administration; the highest concentration in the milk was found to be reached after 2.0 h.

CONCLUSIONS:

DLLME-HPLC was demonstrated to be a simple and rapid method for the determination of NSAIDs in human milk with percentage relative recoveries (%RR) in the range of 93.1-104.6%.

ACKNOWLEDGEMENTS:

This study was supported by a BAP Project of Near East University (SAG-2016-2-022)

REFERENCES:

1. Assadi Y et al., (2006). Journal of Chromatography A, 1116:1-9.

OP-078: COVALENT IMMOBILIZATION OF Γ-GLUTAMYL TRANSPEPTIDASE ON TANNIC ACID MODIFIED MAGNETIC NANOPARTICLES

Daana, J., Turan, E., Tumturk, H.

Gazi University, Faculty of Science, Department of Chemistry, Ankara, Turkey

INTRODUCTION:

In recent years, noticeable achievements have been spent in the development of magnetic nanoparticles(MNPs). Enzymes ability to catalyze reactions and engage in complex syntheses has long made them attractive for use in a multitude of industrial, and research applications(1). This work presents the synthesis and uses surface modified magnetite nanoparticles for the covalent attachment of γ-Glutamyl transpeptidase enzyme. γ-glutamyl transpeptidase (γ-GGT; EC 2.3.2.2) is an enzyme that catalyzes the transfer of the γ-glutamyl group of glutathione to an amino acid or a peptide.

MATERIALS AND METHODS :

Fe_3O_4 MNPs were prepared via well-known co-precipitation reaction. Subsequently, the surface of magnetic nanoparticles was modified by employing a plant-derived polyphenol(rich with hydroxylic groups) tannic acid as the structure-directing agent as well as the stabilize to enhance the ability to immobilize GGT covalently.

RESULTS:

GGT was covalently immobilized on tannic acid modified MNPs after exposing nanoparticles to pH 9.2. Enzyme loading was 92.98% onto the MNPs. The immobilized enzyme demonstrated maximum catalytic activity at pH 8.5 and 60 °C. The kinetic parameters of free and immobilized enzyme were evaluated according to the Lineweaver–Burk plot (KM) 0.907 mM and 1.19 mM, respectively.

CONCLUSION:

in this study, MNPs were successfully prepared by co-precipitation reaction. Subsequently, the surface of magnetic nanoparticles was modified by Tannic acid.Moreover, the immobilized enzyme shows good durability and could be easily recovered by magnetic separation.

REFERENCES

1. Johnson BJ et al., (2014). Nano Today, 9(1):102-131.
2. Juang TY et al., (2014). Molecules, 19:4997-5012.

OP-079: LARGE VOLUME SAMPLE STACKING IN CAPILLARY ELECTROPHORESIS FOR THE QUANTITATIVE DETERMINATION OF PHENOLIC COMPOUNDS FROM FOOD SAMPLES

[1,2] Memon, AM, [1] Palabiyik, IM, [2] Solangi, AR, [3] Memon, SQ, [3] Mallah, A.

[1]Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey.

[2]University of Sindh, National Centre of Excellence in Analytical Chemistry, Jamshoro, Pakistan

[3]University of Sindh, Dr. M. A. Kazi Institute of Chemistry, Jamshoro,Pakistan.

INTRODUCTION:

Because of these health promoting benefits and biological properties of phenolic compounds, researches are interested in developing different methods for their identification, extraction and separation from natural sources. In the present study, a simple and rapid CZE method was developed and LVSS with polarity switching was applied for the simultaneous separation of naringin, rutin, carnosic acid, apigenin, quercetin, morin and chicoric acid in different food samples. To perform method validation, we used RSM to examine the effect of buffer pH, buffer concentration and applied voltage.

MATERIALS AND METHODS:

CE separations were carried out in an Agilent 1100 (Agilent Technologies, Germany) capillary electrophoresis system equipped with a photodiode array detector and automatic injector. Uncoated fused silica capillaries of 50 µm diameter and 56 cm effective length with extended light path (Agilent Technologies, Germany) were used throughout the experiments. The detection wavelength of 214nm was used and the temperature of capillary was maintained at 25 oC. The background electrolyte (BGE) used for separation was 20 mM borate buffer (pH 9.2).

RESULTS:

Optimized LVSS conditions: sample injection at 100 mbar for 20 sec, matrix removal at -20 kV for 6 sec, followed by separation with 20 mM borate buffer (pH 9.2) at +16 kV. Under these optimized conditions, all seven analytes were baseline separated within 20 min. LVSS resulted in a two fold increase in peak areas (when compared with same concentration injected during 10 s) and three fold increase in peak heights, resulting in considerable improvement in detectability. The developed and optimized methods were applied to determine phenolic compounds from 18 different samples.

CONCLUSIONS:

In this method, we have developed a fast, reliable, sensitive and accurate CZE-LVSS method for the simultaneous determination of naringin, rutin, carnosic acid, apigenin, quercetin, morin and chicoric acid from a number of food samples.

ACKNOWLEDGEMENTS:

This study was supported by a grant from TUBITAK – 2216 program.

OP-080: THERMOSENSITIVE-PNVCL-BASED HYBRID HYDROGELS FOR BIOMEDICINAL APPLICATIONS

Durkut, S., Elcin, YM., Elcin, AE.

Ankara University, Faculty of Science, Tissue Engineering, Biomaterials and Nanobiotechnology Laboratory, Ankara, Turkey

INTRODUCTION:

Stimuli-responsive hydrogels are used to deliver drugs with safe and effective concentrations in response to an external stimulus (1). Because of the difference between the normal and pathological tissues, which are accompanied with local temperature increase by 1–5°C, thermosensitive polymers may have the potential to modulate drug release. Hybrid biopolymer systems, composed of a thermosensitive synthetic polymer and a natural-origin hydrogel can produce a biomimetic system with potential biomedicinal applications (2), biotechnology and tissue engineering (3). Poly(N-vinylcaprolactam) (PNVCL) is a biocompatible thermosensitive polymer with a LCST of ~32oC. In this study, PNVCL based hybrid hydrogels were evaluated in terms of composition, structure, release and mechanical properties.

MATERIALS AND METHODS:

PNVCL-COOH was synthesized by free radical polymerization, and then conjugated with the natural biopolymers by utilizing covalent bonding between the carboxylic acid groups at the chain ends and amine groups of the polymers using the EDC/NHS cross-linker. Phase transition temperatures were determined by measuring the optical transmittance at 480 nm over the temperature range of 20-50oC. The swelling and release kinetics of the biopolymers were determined. To assess the in-vitro release properties of the PNVCL based scaffolds, experiments were carried out with a model protein (bovine serum Ibümin, BSA etc.) and a model drug (Doxorubicin, Dox, a widely used anticancer agent etc.) at two different temperatures of 4oC and 40oC.

RESULTS:

The PNVCL-based biopolymers exhibited a distinct phase transition temperature between 32 and 38oC. Drug release was influenced by environmental temperature in terms of the change in the hydrophilic-hydrophobic character, gel forming and swelling properties of the hybid biopolymer. In this way, the thermosensitive PNVCL-based hydrogel underwent reversible structural transitions from a closed state to an open state with the help of external temperature stimuli, giving on-off switches for modulated drug delivery.

CONCLUSIONS:

Thermosensitive PNVCL with various combinations of natural polymers may have potential in bio-relevant applications.

ACKNOWLEDGEMENTS:

This work was supported by the Ankara University Research Fund (No.14B0430002).

REFERENCES

1. Peppas NA (2004). Adv. Drug Delivery Rev., 56:1529-1531.
2. Klouda L, Mikos AG (2008). Eur. J. Pharm. Biopharm., 68:34-45.
3. Lee B et al., (2013). Acta Biomater., 9:7691-7698.

OP-081: EXPERIMENTAL DESIGN APPROACH TO OPTIMIZE HPLC SEPARATION OF ACTIVE INGREDIENTS, PRESERVATIVES AND COLORANTS IN SYRUP FORMULATION

Dinc Zor, S., Asci, B., Aksu Donmez, O., Hacimustafa, O.

Yildiz Technical University, Department of Chemistry, Davutpasa Campus, Istanbul, Turkey

INTRODUCTION:

In this study, a simple, accurate, precise and rapid HPLC method was developed for the simultaneous analysis of pseudoephedrine HCl (PSE) and guaifenesin (GU), along with synthetic preservatives, methyl paraben (MP) and propyl paraben (PP), and colorants, ponceau 4R (PO) and sunset yellow (SY) in syrup samples. Optimum conditions of HPLC separation were performed with Box-Behnken experimental design. Four independent variables of the separation were pH (6.0, 6.5, and 7.0) and flow rate of the mobile phase (2.0, 2.2 and 2.4 mL/min) and mobile phase ratios for the first and second gradient elution (75, 80, and 85% for Gradient 1 and 50, 55, and 60% for Gradient 2 in terms of phosphate buffer percent, respectively). Resolution between adjacent peaks was used for the response of the variables.

MATERIALS AND METHODS:

Chromatographic separation was achieved using reversed phase C18 column (4.6 mm x 250 mm x 5 µm particle size) and the eluents were monitored via a diode array detector at 215 nm.

RESULTS:

According to the results of the optimization procedure, the optimum variables were found to be pH, 6.3; flow rate, 2.4 mL/min; mobile phase ratios for gradient 1 and 2, 85 and 60%, respectively. Therefore, chromatographic procedure of the method was determined with 0.025M phosphate buffer, pH 6.3, acetonitrile gradient that follows 0–4 min, 85 : 15 (v/v); 4–9 min, 60 : 40 (v/v) and 9-10 min, 30 : 70 (v/v). The mobile phase flow rate was 2.4 mL/min and the injection volume was 20 □L in all the chromatographic runs.

CONCLUSIONS:

Under these conditions, the developed method was validated in accordance with ICH guidelines and the method was successfully applied for the simultaneous determination of PSE, GU, MP, PP, PO and SY in a commercial syrup sample.

ACKNOWLEDGEMENTS:

This work was financially supported by Yildiz Technical University Research Foundation (Project No: FAP-2017-3118).

OP-082: MIR-185-5P RESPONSE TO USNIC ACID INHIBITS THE PROLIFERATION IN BREAST CANCER CELL

Değerli, E., Torun, V., Yangın, S., Cansaran Duman, D.

Ankara University, Biotechnology Institute, Central Lab., Ankara, Turkey

INTRODUCTION:

Breast cancer (BC) is one of the major deadly cancer type among women. Due to side effects of commercially drugs and other treatments, the usage of alternative biological sources becomes has quite significantly important in effective treatment of BC. Usnic acid (UA) is one of the secondary metabolites extracted from lichen species. In recent years, increasing evidence shows that dysregulated miRNAs serve function as key regulators of biological processes including proliferation, differentiation, apoptosis etc. (1, 2). In our previous study, microarray experiments showed that miR-185-5p were specifically responsive to UA in BT-474 BC cell. In this study, we aimed to investigate the antiproliferative effect of miR-185-5p in BC cell and to provides a new target for the treatment of BC.

MATERIALS AND METHODS:

BT-474 cell was seeded in a 96-well plate (5x103/ well) and were transfected with miR-185-5p using Transfection Reagent (Qiagen) according to the manufacturer's instructions. Transfection of miR-185-5p were performed at different concentrations as 0, 5, 10, 25, 50, 75 and 100 nM in BT-474 cells. The miR-185-5p transfected cells incubated for 24 and 48 h. After the incubation time, total of 20 µl MTT reagent was added to the BT-474 cells for the evaluation of antipoliferative effect. The absorbance of the plate was measured using a microplate reader at the 570 nm.

RESULTS:

Results from the our study demonstrated that the transfection of miR-185-5p mimics inhibited the cell viability in BT-474 breast cancer cells. Further, we showed that the cell viability was reduced by approximately 30 % in 48 h after 30 nM miR-185-5p mimic was transfected to BT-474 cells.

CONCLUSIONS:

In present study, for the first time we revealed the antiproliferative effect of miR-185-5p in breast cancer. miR-185-5p has potent inhibitory effect on breast cancer cell proliferation. Therefore, miR-185-5p may represent a novel therapeutic target for the treatment of breast cancer. However, further research is needed to investigate of miR-185-5p at molecular level. Thanks to these investigations, new therapies based on miR-185-5p can be developed and miR-185-5p might be used for treatment of breast cancer in the future.

ACKNOWLEDGEMENTS:

We thank Ankara University, Management of Scientific Research Projects (Project no. 17L0415002 and 15B0415001), for the financial support.

REFERENCES:

1. Iorio MV, Croce CM (2012). Carcinogenesis, 33(6):1126–33.
2. Pinweha P, Rattanapornsompong K, Charoensawan V, Jitrapakdee S (2016). Comput Struct Biotechnol J, 14:223–233.

OP-083: DRUG-DRUG INTERACTIONS IN PEDIATRIC PATIENTS TAKING CLARITHROMYCIN

[1] Macit, C., [2] Taner, N., [2] Simsek, A., [3] Olguner Mercanoglu, HG.

[1] Istanbul Medipol University, Department of Pharmacology, Istanbul, Turkey

[2] Istanbul Medipol University, Department of Clinical Pharmacy, Istanbul, Turkey

[3] Saglik Bilimleri University, Department of.Pharmacology, Istanbul, Turkey

INTRODUCTION:

Antibiotics are one of the most prescribed drugs among the pediatric patients. Usually, penicillins are used for pediatric populations, however, in some cases such as penicillin allergy, clarithromycin is preferred because of its safety profile when compared with other antibiotics. The objective of this study was to examine the drug-drug interactions associated with clarithromycin in the pediatric patients.

MATERIALS AND METHODS:

This study was performed at the community pharmacies located in the Uskudar and Umraniye during 10 months. Totally, 100 (60 males and 40 females) pediatric patients who were prescribed with clarithromycin, were included into the study. Their prescription was examined in terms of clarithromycin interaction by the use of RxMedia Pharma 2017 during their visit to the pharmacy. Finally, the obtained data was analysed with SPSS v22 program and the value of $p<0.05$ was considered as statistically significant.

RESULTS:

Overall, the results showed that the rate of drug-drug interaction was 16%, and no significant relationship between the gender and drug-drug interaction rate was found. Among 3 drugs with high drug interactions, lidocaine (cause QT prolongation) has been written 3 times with claritromycin in the same prescription. Overall, 68,75% of the drug-drug interactions were occured by use of other drugs while 31,25% were caused by clarithromycin use.

CONCLUSIONS:

In conclusion, health workers, the patients and their relatives should be trained on the prevention of drug-drug interactions and the adverse effects of multi-drug use (polypharmacy). Moreover, more importance should be given to the pharmacovigilance studies.

REFERENCES:

1. Hersh AL, Shapiro DJ, et al., (2011). Shah SSPediatrics, Dec; 128(6):1053-61.

OP-084: DEVELOPMENT AND CHARACTERIZATION OF COMPOSITE SCAFFOLDS

Koc Demir, A.

Ankara University, Faculty of Science, Tissue Engineering, Biomaterials and Nanobiotechnology Laboratory, Ankara, Turkey

INTRODUCTION:

Development of an ideal scaffold for bone tissue engineering applications is an ongoing goal for the biomaterials scientists. Natural polymers are generally preferred to synthetic ones due to their biological response and degradation properties in the human body (1). Among numerous natural polymers, chitosan (C) and gelatin (G) are considered as promising polymers because of their non-toxicity, excellent biocompatibility and biodegradability (2). Trace elements found in bone (magnesium, zinc, strontium) are known to be necessary for healthy growth, development and functioning of the bone. Developing functional biomaterials capable of releasing osteogenic ions is crucial to promote bone formation around the implant. Montmorillonite (MMT) may be considered as an 'ion reserve', and can be enriched with osteogenic ions, such as Mg, Sr, or Zn to enhance its osteogenic capacity. In this study, MMT was modified with Mg2+ before blending with gelatin and chitosan to produce a promising biomaterial for bone tissue engineering applications.

MATERIALS AND METHODS:

MMT with a cation exchange capacity (CEC) of 102 meq/100 g was obtained from Unye Bentonite Company (Ordu, Turkey). Composite scaffolds were produced through freeze drying method. Briefly, the G/C solution was prepared and then required amount of Mg-modified and non-modified MMT were introduced to the solution and stirred overnight to get a perfectly homogenous solution. Then, glutaraldehyde solution was added dropwise into the solution with vigorous stirring at 40°C. The obtained suspension was poured into a plastic mold and frozen; then lyophilized in a freeze dryer. The sponges were soaked in 1M NaOH for insolubilization, rinsed a few times with double-distilled water and lyophilized again. The synthesized scaffolds were characterized by XRD, FTIR, TGA and SEM. The release of Mg2+ from scaffolds into cell culture medium was determined by ICP-OES. The pore size distribution of scaffolds was determined by MIP.

RESULTS:

The results of FTIR and XRD confirmed intercalation of G/C into MMT layers. TGA studies concluded that the MMT in polymer matrix promoted the thermal degradation of the matrix. Morphology results of scaffolds had highly porous morphology with interconnected pores.

CONCLUSIONS:

The data suggest that G/CS/MMT composite scaffold may be a suitable option for bone tissue engineering research.

REFERENCES

1. Thein Han WW, Misra RDK (2009). Biomaterialia, 5:1182.
2. Carreira AS et al., (2010). Carbohydrate Polymer, 80:618–630.

OP-085: DEVELOPMENT OF A VALIDATED HPLC METHOD FOR DETERMINATION OF OLANZAPINE AND ARIPIPRAZOLE IN HUMAN PLASMA

Yeniceli Ugur, D.

Anadolu University, Faculty of Pharmacy, Department of Analytical Chemistry, Eskişehir, Turkey

INTRODUCTION:

In the present study, a HPLC method was developed and validated for determination of olanzapine (OLA) and aripiprazole (ARI) in spiked human plasma considering their combined use for treatment of drug-resistant schizophrenia patients (1, 2).

MATERIALS AND METHODS:

Separation was achieved on a monolithic column (Rp-18, 100-4.6 mm) set at 35°C with a flow rate of 0.8 ml/min. Gradient elution was performed with a mobile phase consisting of phosphate buffer (pH 3.14, 20 mM) and acetonitrile. Carbamazepine was used as internal standard. Detection was performed at 255 nm. Fractional factorial design and Box-Behnken design were used during optimization studies.

RESULTS:

Retention times of OLA and ARI were 2.34 and 6.90 minutes, respectively. The method was linear in the range of 0.125-50.0 µg/ml for OLA and 0.500-50.0 µg/ml for ARI. The quantification limits for OLA and ARI were found 0.0686 and 0.4984 µg/ml, respectively. The method was found accurate and precise based on recovery (99-102%), and RSD (<2%) values. Robustness of the method and the stability of analytes were also investigated.

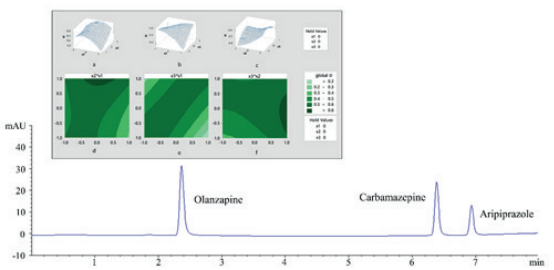


Figure 1. The chromatogram of OLA and ARI in standard solution. Counter plot and surface plot graphics are represented above.

CONCLUSIONS:

In this study, a HPLC method for the simultaneous determination of OLA and ARI was developed and validated for the first time.

ACKNOWLEDGEMENTS:

This work was supported by Research Council of Anadolu University, Project No: 1705S168. The authors thank Assoc. Prof. Dr. Erol Şener for technical support.

REFERENCES:

1. Duggal HS (2004). The Canadian Journal of Psychiatry, 49(2):151-151.
2. Chen CH, Huang MC, Lu ML (2007). Journal of Clinical Psychopharmacology, 27(5): 516-517.

OP-086: URINARY TGF-B1 AND SERUM NADP+/NADPH RATIO OF TYPE 2 DIABETES MELLITUS PATIENTS AND THEIR CORRELATION WITH UACR

Sauriasari, R., Nurtanio, BW., Pratiwi, MY.

University Indonesia, Clinical Pharmacy, Faculty of Pharmacy, Depok, Indonesia

INTRODUCTION:

Hyperglycemia conditions in diabetes mellitus can activate reactive oxygen species (ROS) mainly through activation of NADPH oxidase (NOX), which further will transcribe TGF-β1 (1-3). As a fibrogenic cytokine, TGF-β1 is considered as a key mediator in diabetic nephropathy (1). This study aimed to confirm the activity of NOX by measuring NADP+/NADPH ratio and TGF-β1 in serum of type 2 diabetes mellitus patients.

MATERIALS AND METHODS:

This was a cross sectional study undertaken in April 2017 and approved by the Ethical Committee. Blood dan urine samples were collected from 89 type 2 diabetes outpatients (62 normoalbuminuric and 27 albuminuric patients) at Pasar Minggu Community Health Center and 10 non-diabetes volunteers as control. Urinary TGF-β1 was measured by ELISA, NADP+ and NADPH by colorimetric assay kit and urine albumin to creatinine ratio (UACR) was measured in an accredited laboratory.

RESULTS:

There was no statistical difference in urinary TGF-β1 concentrations ($p = 0.790$) of the three group samples, but there was increasing of concentrations of urinary TGF-β1 in albuminuria conditions. Serum NADP+/NADPH was higher in albuminuria (1.40) rather than normoalbuminuria (1.24) and non-diabetic subjects (0.97) ($p<0.001$). In addition, no correlation between urinary TGF-β1 with UACR in normoalbuminuria and albuminuria groups ($r = -0.079$; $p = 0.462$). However, there was a correlation between NADP+/NADPH serum ratio with UACR in the same groups ($r = 0.297$; $p = 0.008$).

CONCLUSIONS:

There was a significant increased of serum NADP+/NADPH, but not urinary TGF-β1 in type 2 diabetes mellitus patients, especially patients with albuminuria. Increased activity of NOX might play a role in the mechanism of albuminuria in type 2 diabetes mellitus, thus potential to be a targeted therapy for preventing diabetic nephropathy in early stage.

ACKNOWLEDGEMENTS:

This study was supported by PITTA Grant, Directorate of Research and Community Engagement) Universitas Indonesia and PUPT Grant, Ministry of Research and Higher Education, Indonesia for the financial support. We also would like to gratitude Pasar Minggu Community Health Center and Prodia Clinical Laboratory who supported this study.

REFERENCES:

1. Thomson SE, Mclennan SV, Twigg SM (2006). Expert Rev Cin Immunol, 2(3)
2. Asaba K., Tojo A., Onozato M., Goto A., Quinn M., Fujita T., Wilcox C (2005). Kidney International, 67(5):1890-1898.
3. Chen S., Meng X., Zhang C (2013). Biomed Research International, 1-7.

OP-087: EVALUATION OF RATIONAL ANTIBIOTIC USE IN A CHILDREN'S HOSPITAL.

[1] Ozdemir, N., [1] Kara, E., [2] Buyukcam, A., [2] Aykac, K.,[1] Celiker, A., [1] Demirkan, K., [2] Cengiz, AB., [2] Kara, A.

[1]Hacettepe University, Department of Clinical Pharmacy, Ankara, Turkey

[2]Hacettepe University, Department of Pediatric Infectious Diseases, Ankara, Turkey

INTRODUCTION:

Upon introduction into medicine in the 1940s, antibiotics have been centered in modern healthcare. Nowadays, they are the most commonly used drug group throughout the world. Unfortunately in terms of antibiotics consumption Turkey leads Europe. In this study, it was aimed to evaluate antibiotic related medication errors in pediatric inpatients' service.

MATERIAL AND METHODS:

This study was carried on at Hacettepe University Ihsan Dogramacı Children's Hospital. It is a tertiary care hospital with 250 acute-care beds and 215,000 admissions per year. It includes a bone-marrow transplantation unit, newborn intensive care unit, pediatric intensive care unit and cardiovascular surgery intensive care unit. On November 16, 2016,

hospitalized patients' orders were evaluated regarding to rational antibiotic use by point prevalence method by two clinical pharmacists and three pediatric infectious diseases physicians. Antibiotic related drug-drug interactions, dose accuracy, and administration time were evaluated.

RESULTS:

At the time of the study 89 inpatients were using antibiotics. Median age was 42 months (range 1 to 226 months) and 40 (44.9%) of the patients were female. Twenty-one (23.6%) of these patients were in surgical units and, 68 (76.4 %) were in pediatric medicine units. When evaluated for antimicrobial drug use, 64% of the patients were using at least one antimicrobial drug. The median number of antimicrobial drugs used in surgical services was 2 (range: 1-3) and in pediatric services was 2 (range: 1-8). There were no statistically significant differences between the surgical and pediatric services in terms of the number of antimicrobial and antibacterial drugs ($p > 0.05$). Twenty nine patients' orders had medication errors. Twelve patients' antibiotic orders had antibiotic related errors, and total of 17 inappropriate treatments (2 drug-drug interactions, 3 administration time errors, 12 dose errors) were observed.

CONCLUSIONS:

Evaluation of antibiotic use in pediatric inpatients' service by a clinical pharmacist in terms of drug related problems such as drug interactions, side effects and prescribing errors will improve treatment-related outcomes of the patients. Clinical pharmacists' involvement in the multidisciplinary team will alleviate physicians' increased workload.

ACKNOWLEDGEMENT

The authors would like to thank all patients and their parents.

REFERENCES:

1. Kaushal R, et al., (2001). Medication errors and adverse drug events in pediatric inpatients. JAMA, 285 (16):2114-120.

OP-088: PREPARATION AND CHARACTERIZATION OF ION EXCHANGE RESIN COMPLEX OF DIDANOSINE

Inal, O., Akman, R.

Ankara University, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Didanosine is an antiretroviral drug used in the treatment of HIV. Although it has lower toxicity than zidovudine, didanosine has limited use due to the low bioavailability caused by hypoxanthine degradation in the acidic environment and the instability problem due to the enolic structure (1). Didanosine used to apply orally by providing an alkaline environment and nowadays the only marketed form is enteric-coated granule.

In this study, we aimed to prepare ion-exchange resin complex of didanosine in order to enhance the acid stability and to obtain intestinal drug delivery.

MATERIALS AND METHODS:

Didanosine was converted to -Na+ form in order to produce a complex with Amberlite CG-50 which is a weak acidic resin consisting –COOH groups. The drug-resin complex was produced by batch method in pH 7.4 HEPES medium (2). Loading capacity was evaluated during process. Characterization of Na-didanosine was evaluated by XRD and HPLC. Drug-resin complex was evaluated by zeta potential, particle size, FTIR and SEM analysis. The drug release from the complex was studied using dialysis bag for 2 hours at pH 1.2 and for 6 hours at 6.8. UV spectrophotometric method at 250 nm was used for drug assay.

RESULTS:

As converting didanosine to the Na+ form, affinity for resin binding sites were provided and drug was complexed with Amberlite with a drug loading capacity of 30%. The best results were obtained by mixing for 30 minutes in a pH-controlled environment using HEPES 7.4, which provides ionization for both resin and drug. Formation of Na+ salt and drug-resin complex was confirmed by the decrease in zeta potential. The characteristic peaks for both of drug and resin were observed by FTIR and complex formation was confirmed by SEM. Amount of didanosine released from the complex in pH 1.2 medium was about 3% within 15 minutes. This released amount could be due to unbound drug at the surface of resin. Due to the ionization of drug and resin in pH 6.8 approximately 30% of drug was released within 6 hours in this medium. Ionic interaction of Na+ at the environment may be responsible of the release profile and amount (3).

CONCLUSIONS:

Didanosine was loaded onto Amberlite resin at about 38% and this complex was carried drug from acid medium by ionic bonding with its -COOH functional group. Drug release at gastric pH value was negligible due to adsorption of free drug onto the resin, and the drug was release was approximately 15% for 4 hours in pH 6.8. The released amount of didanosine can be modified by increasing loading capacity of resin or using resins with different properties such as swelling and/or functional groups in further studies. However, results give rise to thought that preparation of Na-didanosine resin complexes can be used as drug delivery systems in order to minimize the gastric degradation and to obtain intestinal drug delivery.

REFERENCES:

1. Anderson BD, Wygant MB et al. Int. J Pharm. Vol 45, 27-37, 1988.
2. Jeong SH, Park K. Int. J Pharm. Vol 361, 26-32, 2008.
3. Akkaramongkolporn P, Wongsermsin K et al. AAPS Pharm Sci Tech. Vol 11(3), 1104-1114, 2010.

OP-089: MALDI ORBITRAP DETECTION AND IDENTIFICATION OF SIMVASTATIN AND METABOLITES IN THE RAT TISSUE

Yin, W., Alwabli, R., Rahman, AFM., Kadi, A.

King Saud University, Department of Pharmaceutical Chemistry, College of Pharmacy, Riyadh, Saudi Arabia

INTRODUCTION:

Simvastatin, a 3-hydroxy-3-methylglutaryl coenzyme A(HMG-CoA) reductase inhibitor, is a commonly sold hypolipidemic drug (1). The metabolic profiling of simvastatin has been done using some conventional technique like LC-MS (2), yet so far no studies have been reported for complete study of distribution of this drug and its metabolites, which might be due to its trace amount of metabolites in complex endogenous background. MALDI-LTQ Orbitrap XL provides high resolution, high mass accuracy and high sensitivity, which allows better detection of desired analytes in the background of matrix and endogenous compounds, thus was used to determine the distribution for simvastatin (SV) as well as its metabolites in selected rat tissues and biological matrices in this study.

MATERIALS AND METHODS:

Tissue samples (brain, liver, lung, heart, and kidney) and biological matrices (blood, urine, and feces) were collected from Sprague-Dawley rats 1 hour after the animals had been dosed with 100 mg/kg SV (diluted in 0.5 % methylcellulose) orally using gastric gavage. The extraction of SV and its metabolites was done by mixture of methanol–water (9:1, v/v) for all the samples except for urine extraction, which was done with pure methanol. Mass spectra were collected on a high-resolution MALDI LTQ Orbitrap XL, with 2,5-Dihydroxybenzoic acid (DHB) and 1,5-Diaminonaphthalene (DAN) used as matrix in positive and negative mode, respectively. Dried droplet crystallization was used for the sample deposition (triplicates) on the target plate. Xcalibur software was used for data analysis.

RESULTS:

SV was administerd in 6 rats and altogether 13 metabolites were identified in different biological samples. A list of some major metabolites of simvastatin detected by MALDI-LTQ-Orbitrap XL showing their accurate mass, elemental compositions, possible metabolic reactions and the list of rat samples containing particular metabolites is given below. It is worth noting that no metabolites were detected in rat brain samples.

No	AM $[M+H]^+$/ $[M-H]^-$	Elemental Composition	Proposed Metabolic Reaction	Tissue/ biological fluid distribution
M1	$[M+H]^+$ 435.27414	$C_{25}H_{38}O_6$	SV Hydroxylation	liver, heart, kidney, lung, serum, feces, urine
M2	$[M+H]^+$ 449.25330	$C_{25}H_{36}O_7$	SV Oxidation	liver, heart, lung, serum, feces, urine
M3	$[M-H]^-$ 435.27399	$C_{25}H_{40}O_6$	SV Hydrolysis	liver, heart, lung, kidney, serum, feces
SV	$[M+H]^+$ 419.27902	$C_{25}H_{38}O_5$	Parent drug	liver, heart, lung, serum, feces, urine

CONCLUSIONS:

Simvastatin and its thirteen metabolites were detected in high resolution and their distribution over major organs were demonstrated on a MALDI-LTQ Orbitrap XL. At least one metabolite, tentatively assigned as a reduced product, is being reported for the first time.

REFERENCES:

1. Simvastatin. The American Society of Health-System Pharmacists; 2015.
2. Fenne OS. (2003). In vitro studies suggest involvement of CYP2D6 in the metabolism of simvastatin and active metabolites.

OP-090: AXITINIB REDUCE APOPTOSIS IN EXPERIMENTAL CORNEAL NEOVASCULARIZATION MODEL IN RATS.

[1] Canacankatan N., [2] Dinc E., [3] Yalaza C., [4] Antmen ES.

[1]Mersin University, Faculty of Pharmacy, Department of Biochemistry, Mersin, Turkey.

[2] Mersin University, Faculty of Medicine, Department of Ophthalmology, Mersin, Turkey.

[3]Toros University, Vocational School, Department of Medical Services and Techniques, Mersin, Turkey.

4Mersin University, Vocational School of Medical Services, Mersin, Turkey.

INTRODUCTION:

Ischemia, chemical burns, infection, trauma and inflammation cause corneal neovascularization (NV). Abnormal vascularization, decreases in visual acuity by blocking the light due to the corneal scarring and leads permanent vision loss (1,2). This study investigated the efficacy of topical application of vascular endothelial growth factor (VEGF) receptor inhibitor, Axitinib on apoptosis in experimental corneal NV model in rats. Caspase-9 was determined for mitochondria-dependent pathways, caspase-8 was

evaluated for death receptor-induced pathways and caspase-3 was investigated for overall apoptosis (3,4).

MATERIALS AND METHODS:

Experimental corneal NV model was formed by silver nitrate cauterization. 6 groups (n=7) were included as Control; Corneal NV; Corneal NV + DMSO; Corneal NV + 0,04% Axitinib; Corneal NV + 0,08% Axitinib and Corneal NV + 0,24% Axitinib. Treatment with Axitinib eye drops of varying concentrations were carried out four times a day for five day in right eye. The aqueous humor was collected and caspase -3, -8 and -9 as apoptotic markers were determined by colorimetric methods according to the assay instructions.

RESULTS:

Caspase -3 and -8 enzyme activities were significantly suppressed by 0,04%, 0,08% and 0,24% Axitinib whereas no effect was observed on Caspase -9.

CONCLUSIONS:

Axitinib reduced apoptosis by suppressing caspase-8 enzyme activity, suggesting that it has potential effect on the death receptor induced pathway of apoptosis.

ACKNOWLEDGEMENTS:

1. This study was supported by a grant of Mersin University Research Foundation (2016-2-AP3-1922)

REFERENCES:

1. Chang et al., (2001).Curr Opin Ophthalmol, 12:242-249.
2. Jin-Hong et al., (2012) Surv Ophthalmol, 57: 415–429.
3. Reed JC (2000). J Pathol, 157:1415–1430.
4. Elmore S (2007). Toxicol Pathol, 35: 495–516.

OP-091: EVALUATION OF DRUG-DRUG INTERACTIONS OF ANTIHYPERTENSIVE DRUGS

[1] Kandemir, EA., [1] Balli, FN., [1] Kara, E., [1] Demirkan, K., [2] Sain Guven, G.

[1]Hacettepe University,Faculty of Pharmacy, Department of Clinical Pharmacy, Ankara, Turkey

[2]Hacettepe University, Faculty of Medicine, Department of Internal Medicine, General Internal Medicine, Ankara, Turkey

INTRODUCTION:

Antihypertensives are one of the most commonly used drugs. Due to co-morbidities, polypharmacy is common among the hypertensive patients. The patients with polypharmacy are at risk of drug-drug interactions (DDIs). Potential DDIs could be evaluated by different online databases and the results of these databases may vary from one to another (1,2). The aim of this study was to demonstrate and to analyze the difference between three different drug-drug interaction databases.

MATERIALS AND METHODS:

Hospitalized patients were followed up between 25 December 2017 and 15 March 2018 in the university hospital general medicine ward. Only the patients who were using antihypertensive drugs for any reason were included. The drugs used by the patients were evaluated by 3 different online databases (Micromedex®, Medscape® and Drugs.com®).

RESULTS:

Total of 42 patients [24 (%57.1) females)] were included in the study and the mean age of the patients was 65.3±17.97 years. Thirty of the patients (71.4%) were suffering from hypertension and the remaining patients were taking antihypertensive drugs due to different problems. The patients had a median 4 (range: 1-9) different disease (including hypertension). Twenty-two (52.4%) of the them were using beta-blocker, 21 (50%) were using angiotensin II receptor blocker (ARB)/angiotensin-converting enzyme inhibitors (ACEI), 18 (42.9%) were using calcium channel blocker (CCB), 17 (40.5%) were using diuretic and 5 (11,9%) were using alpha blockers. Patients were using median 2 (1-5) different antihypertensive drugs (range: 1 - 5) and 9 (range: 1-18) non-antihypertensive drugs. According to Micromedex, Medscape and Drugs.com databases 29 (%59), 37 (%88.1) and 36 (%85.3) patients had potential DDIs, respectively.

CONCLUSIONS:

The patients using antihypertensive drugs are relatively older and have numerous comorbidities and comedications. More than half of the patients have a potential to have DDIs. Clinicians should be aware of the rate of determination of DDIs and that the categorizations of DDIs differ between online databases.

ACKNOWLEDGEMENTS:

This study was not supported by any grant.

REFERENCES:

1. Elliott WJ (2006). Drug Interactions and Drugs That Affect Blood Pressure. The Journal of Clinical Hypertension, 8: 731-737
2. Maas R, Böger RH (2003). Antihypertensive therapy: special focus on drug interactions. Expert Opin Drug Saf. 2003 Nov;2(6):549-79.

OP-092: PREPARATION, OPTIMIZATION AND IN VIVO EVALUATION OF HYDROQUINONE LOADED MICROEMULSION FORMULATIONS FOR MELASMA TREATMENT

[1] Caglar, ES., [2] Pekcan, AN., [3] Okur, E., [4] Ayla, S.,[1] Ustundag Okur, N.

[1]Istanbul Medipol University, School of Pharmacy, Department of Pharmaceutical Technology, İstanbul, Turkey

[2]Istanbul Medipol University, Graduate School of Health Sciences, Department of Clinical Pharmacy, Istanbul, Turkey

[3]University of Anadolu, School of Pharmacy, Department of Pharmacology, Eskişehir, Turkey

4Istanbul Medipol University, School of Medicine, Department of Histology and Embryology, İstanbul, Turkey

INTRODUCTION:

Melasma is an acquired disorder of pigmentation that presents as symmetric darkening on the face. It has a multifactorial etiology and influencing factors include increased UV exposure, pregnancy, cosmetics, genetic factors, endocrine factors, and hormonal therapy (1, 2). In our study, we aimed to develop and evaluate the strengthening of penetration to the epidermis of the hydroquinone (HKN) loaded new alternative drug carrier systems for the treatment of melasma.

MATERIALS AND METHODS:

For the preparation of hydroquinone loaded microemulsions, isopropyl myristate as the oil phase, Cremophor EL, Span 20, Span 80 and Tween 20 as surfactant, ethanol as co-surfactant, distilled water as aqueous phase were used. In vitro drug release studies were performed. Conductivity, viscosity, pH, refractive index, zeta potential, PDI, droplet size were measured in terms of characterization studies. Furthermore, a skin irritation experiment was achieved with healthy BALB-c mice. Mice were divided into five groups: HKN loaded microemulsion 1 (M1HKN), HKN loaded microemulsion 2 (M2HKN), HKN loaded cream (CHKN), HKN solution (SHKN), and Control group (serum physiologic, (SF) Histopathological analysis of the formulations on mice skin was carried out.

RESULTS:

As results of the study, it was measured that conductivity between 16.667 ± 5.774 and 43.333 ± 5.774, viscosity between 8.97 ± 0.082 and 45.67 ± 2.259, pH between 3.3 ± 0.436 and 5.7 ± 0.2 and refractive index between 1.4032 ± 0.0002 and 1.4299 ± 0.0002. Formulations showed that zeta potential between -0.461±0.009 and 0.359±0.223, PDI between 0.08±0.02 and 0.196±0.067,and droplet size between 24.27±3.559 and 324.9±16.8 nm. Furthermore, in vitro drug release studies showed that formulation M2 released 87.405 % of the drug at the end of the 24h. According to the results of histopathological analysis (Figure 1), the stratum corneum layer turned thinner after application of formulations; nevertheless, it is not observed any visible difference in skin morphology after 24h.

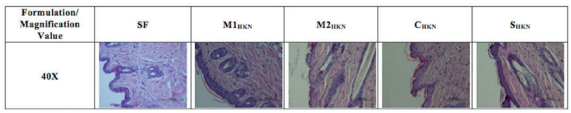


Figure 1: Formulation (SF, M1HKN, M2HKN, CHNK, SHNK) applied mice skin. 40 x (magnification value), H&E (Hematoxylene and Eosin).

CONCLUSIONS:

According to results of our study, hydroquinone loaded microemulsions can be seen as a promising alternative for the treatment of melasma disease.

REFERENCES:

1. Cohen PR (2017). Medical Hypotheses., 101:1-
2. Hussain S et al., (2016). Journal of Pakistan Association of Dermatologists. 26(1): 31-34.

OP-093: TWO DIFFERENT SPECTROPHOTOMETRIC METHODS FOR THE DETERMINATON OF METHIMAZOLE IN TABLET PREPARATIONS

Dermis, S., Beyaztas, S.

Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Thyroid disorder refers to abnormalities in the functions of the thyroid gland which is a hormone-releasing organ. Methimazole, an antithyroid agent, has gained a distinct value in the medical world because it is very effective in hyperthyroidism (1,2). We aim to develop a fast analysis method to quantify methimazole in tablets.

MATERIALS AND METHODS:

Two different spectrophotometric methods, based on direct absorbance measurement and first derivative absorbance measurement were performed for the quantitative analysis of the methimazole in commercial tablets. The linear working range of methimazol for both methods were 2.0-24.0 µg/mL. The solutions were prepared in methanol and their absorbance spectra were recorded in the range of 200.0-320.0 nm. The direct absorbance spectra and first derivative spectra of the calibration set were given in Figure 1.

The absorbance values used to obtain the calibration curves of direct and first derivative methods were at 260.0 nm and 268.6 nm, respectively. The correlation coefficiens were calculated as 0.99897 and 0.98898, respectively. These two methods were validated by

recovery and standard addition studies. Then, the commercial samples were analyzed by the proposed methods.

RESULTS:

Mean recovery results for standard addition samples were found as 103.3 and 98.0 for direct and first derivative methods, respectively. Ten tablets was analyzed by the proposed methods and succesful results were obtained.

CONCLUSIONS:

Two different spectrophotometric methods were developed by means of direct absorbance spectra and first derivative absorbance spectra. Both methods were validated and used to analyse methimazol in tablets and satisfactory results were obtained.

REFERENCES:

1. Fumarola et al., (2010). Experimental and Clinical Endocrinology & Diabetes, 118:678-684.
2. Abraham et al., (2005). Eurepean Journal of Endocrinology, 153:489-498.

OP-094: BRASSININ SYNERGISTICALLY INDUCED THE ANTICANCER EFFECTS OF IMATINIB IN SW480 COLON CANCER CELLS

Ozkan, E., Bakar Ates, F.

Ankara University, Faculty of Pharmacy, Department of Biochemistry

INTRODUCTION:

Colorectal cancer has been identified as the third most common cancer and the fourth cause of death related with cancer worldwide (1). Hence, treatment of this disease has gained much importance as well as its diagnosis and prevention. Some natural compounds have potent cytotoxic effects against cancer cells. Brassinin, a kind of phytoalexin, is one of the challenging compounds within this scope. Brassinin is supposed to have anticancer effects because of its structure that contains an indole nucleus and a dithiocarbamoyl-aminomethyl moiety (2). Researchers have shown the antiproliferative effects of brassinin on in vivo and in vitro models of colon cancer through the inhibition of the PI3K signaling pathway (3). It has also been demonstrated that brassinin may induce apoptosis by blocking PI3K/Akt/mTOR/S6K1 signaling pathways (4). In the present study we aimed to evaluate the effects of brassinin in combination with imatinib, a clinically used chemotherapeutic drug.

MATERIALS AND METHODS:

The effects of brassinin alone and in combination with imatinib on cell proliferation were determined by MTT assay. The effects of combination therapy on cell cycle arrest and annexin v binding have been measured by cell analyzer. The apoptotic cell population has also been shown by fluorescence imaging studies.

RESULTS:

The results showed that brassinin has significantly inhibited the proliferation of SW480 cells at 50, 100 and 200 μM brassinin in combination with imatinib (14.05 μM), whereas brassinin alone could inhibit cell growth only at 200 μM. Our results also demonstrated that brassinin-imatinib combination has caused a cell cycle arrest at G0/G1 phase and it has significantly increased the apoptotic cell population when compared to control ($p<0.05$).

CONCLUSIONS:

Results of this study indicated that brassinin has synergistically increased the anticancer effects of imatinib in SW480 human colorectal cancer cells. Further studies are required to identify the underlying mechanisms of effects.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-216S129)

REFERENCES:

1. Brenner et al., (2014). Lancet, 383:1490-1502.
2. Mehta et al., (1995). Carcinogenesis, 16:399-404.
3. Izutani et al., (2012). International Journal of Oncology, 40:816-824.
4. Kim et al., (2014). Phytotherapy Research, 28:423-431.

OP-095: PATIENTS' ATTITUDES ON SAFE HANDLING OF ORAL CHEMOTHERAPEUTICS

[1] Aras, E., [1] Tecen Yucel, K., [1] Ozdemir, N., [1] Bayraktar Ekincioglu, A., [2] Aktas, BY., [2] Kilickap, S.

[1] Hacettepe University, Faculty of Pharmacy, Department of Clinical Pharmacy, Ankara, Turkey

[2] Hacettepe Cancer Institute, Department of Medical Oncology, Ankara, Turkey

INTRODUCTION:

Safe handling and appropriate storage of oral chemotherapeutics are crucial for maintaining the success of chemotherapy. It is also important for patients and their caregivers to avoid unexpected and hazardous exposures during treatment. Although guidelines are available for aseptic drug preparation, safe handling and administration of parenterally administered chemotherapy drugs, there are few recommendations issued for safe handling and disposal of oral chemotherapeutics. The aim of this study was to evaluate patients' attitudes in drug usage and handling of oral chemotherapeutics.

MATERIALS AND METHODS:

This study was conducted at an outpatient clinic in the Hacettepe University Oncology Hospital between 29th March and 19th April 2018. The patients who are older than 18 years of age and currently use oral chemotherapeutics were included in the study. The patients were asked 15 questions regarding demographics (age, gender and educational level), drug usage, storage/disposal conditions and hand hygiene in the use of oral chemotherapeutics.

RESULTS:

A total of 24 patients were included, of those 5 (20.8%) were male and the mean (± standard deviation) age was 54.29 (±8.73) years. Among the participants, 11 (45.83%) indicated to have an education on the use of oral chemoterapeutics, of those 9 (81.8%) indicated to have before the chemotherapy initiated. They stated that information was given by nurses (n=7, 63.6%) and doctors (n= 4, %36.3). All patients indicated not to crush / split their medication and 95.8%(n=23) take the dose correctly in terms of timing. About 45.8% and 33.3% of the patients indicated that they wash their hands 'before' and 'after' taking oral chemotherapy drugs, respectively. However, none of the patients use gloves while taking their oral chemotherapy drug. In regards to correct storage of drugs, 87.5% of patients indicated to keep their medicines in their original box and 79.2% stored medicines at room temperature.

CONCLUSIONS:

Unfortunately the concept of rational drug use which includes aspects of safe handling and proper storages/ disposal of medicine, can be ignored by patients and healthcare professionals in routine practice. Therefore, practice standards on each aspects of chemotherapy drug usage should be established and patients should be informed about the correct use of oral chemotherapeutics by healthcare professionals.

ACKNOWLEDGEMENTS:

The authors would like to thank all participating patients and hospital staff at the outpatient clinic.

REFERENCES:

1. Trovato JA, et al., (2014). Oral chemotherapy handling and storage practices among Veterans Affairs oncology patients and caregivers. J Oncol Pharm Practice, Vol. 20(2) 88–92.

OP-096: RATIO DERIVATIVE AND DIFFERENCE SPECTROPHOTOMETRIC TECHNIQUES FOR SIMULTANEOUS DETERMINATION OF CARVEDILOL AND HYDROCHLOROTHIAZIDE IN MARKETED TABLETS

[1] Erk, N., [2] Tiris, G.

[1]Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

[2]Bezmialem Vakif University Faculty of Pharmacy, Department of Analytical Chemistry,Istanbul, Turkey

INTRODUCTION:

Hypertension is the leading risk factor for cardiovascular disease and mortality worldwide. Carvedilol (CAR) and Hydrochlorothiazide (HYD) are used alone or as combination therapy in the treatment of patients whose blood pressure is not adequately controlled with any of the substances alone.

METHODS:

Ratio derivative and difference spectrophotometric techniques were developed for analyzing a binary mixtures of CAR and HYD. In this technique the absorption spectrum of binary mixture was divided by the absorption spectrum of the standard solution. The ratio spectra were recorded. The ratio derivative amplitudes were measured at 236.7 nm for CAR and 261.8 nm for HYD, respectively. On the other hands ,in the ratio difference spectrophotometric technique which measures the difference in amplitudes between 241.3 -285.8 nm for CAR and 226.45 – 269.03 nm for HYD, respectively.

RESULTS:

The calibration curves were linear over the ranges of 2-10 mug mL(-1) and 3 -20 mug mL(-1) for CAR and HYD, respectively. In order to access the validity and applicability of the described method, recovery studies were performed by analyzing synthetic laboratory mixtures of each drug in different ratios. The results obtained were statistically compared to each other and to that of the reported HPLC method. The statistically comparison showed that there is no significant difference regarding both accuracy and precision.

CONCLUSIONS:

The developed methods could be successfully applied for the routine analysis of binary mixtures in quality control laboratories without any preliminary separation steps.

OP-097: INOSITOL- REQUIRING ENZYME 1 (IRE1) INHIBITOR, STF-083010, DOWNREGULATES PROATHEROGENIC GENE EXPRESSION IN BONE MARROW DRIVED MACROPHAGES

[1] Telkoparan Akillilar, P., [2] Tufanli, O., [3] Acosta Alvear, D.,[4] Walter, P., [2] Erbay, E.

[1] Yuksek Ihtisas University, Faculty of Medicine, Department of Medical Biology, Ankara, Turkey

[2] Bilkent University, Molecular Biology and Genetics, Ankara, Turkey

[3]Department of Biochemistry and Biophysics, University of California, San Francisco, CA 9414[3]

INTRODUCTION:

The endoplasmic reticulum (ER) is a central organelle for protein biosynthesis, folding, and traffic (1). Perturbations in any of these functions results in ER stress and aggregation of misfolded/unfolded proteins. Accumulation of unfolded proteins can initiate ER stress and activate the Unfolded Protein Response (UPR) (2). UPR activation is a hallmark of atherosclerotic plaque formation (3). The most conserved ER-resident UPR regulator, inositol-requiring enzyme 1 (IRE1), is activated in lipid-laden macrophages on atherosclerotic lesions. Several lines of evidence support the notion that selective pharmacological targeting of IRE1 is a desirable therapeutic approach for treatment of atherosclerosis. In this study we aimed to investigate the direct contribution of IRE1 to atherosclerotic disease progression.

MATERIALS AND METHODS:

Bone marrows were collected from the tibia and femurs of mice into RPMI-1640 medium and resuspended in RPMI-1640 medium enriched with 15% (vol/vol) L929 conditioned medium and seeded on Petri dishes for 7 d. Then, BMDM cells were treated with STF-083010 60 µ for 6 hours. Total RNA was isolated using Trisure (Bioline). Sequencing libraries for whole-transcriptome analysis were prepared using the ScriptSeq v2 RNA-Seq Library Preparation Kit (Epicentre Biotechnologies) and sequenced in Illumina HiSeq2500 Deep-Sequencer. To estimate the changes in gene expression levels, the number of sequenced reads that align to a gene of interest was then compared among biological samples using Cuffdiff tool.

RESULTS:

We analyzed differentially regulated mRNAs at early time points (6 hours) after IRE1 inhibition. We observed increased expression of 169 genes and decreased expression of 135 genes on IRE1 inhibition. To categorize the affected genes we used the Ingenuity Pathway Analysis (IPA) tool. IPA identified the down-regulation of many important pro-atherogenic genes (such as Il-1β, Ccl2, S100a8, and Mmp9) on inhibition of the steady-state IRE1 activity. We next validated our findings using quantitative (q)RT-PCR method. Our results suggest that the IRE1-XBP1 signaling branch of the UPR maintains the expression of key proatherogenic cytokines and chemokines in macrophages.

CONCLUSIONS:

Our findings suggest that IRE1 plays an important role in atherosclerosis progression. Therefore, pharmacological inhibition of IRE1 represents a promising therapeutic approach to manage atherosclerosis.

REFERENCES:

1. Park SW, Ozcan U (2013). Immunopathol 35(3): 351-73.
2. Walter P, Ron D (2011). Science 334(6059): 1081–1086.
3. Zhou AX, Tabas I (2013). Semin Immunopathol 35(3): 321–332.

OP-098: INFLUENZA VACCINE: WHY WE ARE NOT VACCINATED?

[1] Bahap, M., [1] Kara, E., [1] Bayraktar Ekincioglu, A., [1] Demirkan, K., [2] Unal, S.

[1] Hacettepe University, Faculty of Pharmacy, Department of Clinical Pharmacy, Ankara-Turkey

[2] Hacettepe University, Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Ankara-Turkey

INTRODUCTION:

Despite recent widespread awareness campaigns on influenza vaccination in Turkey, vaccination rate in adult population remains low due to misperception among the public. Therefore, this study aimed to explore perceptions and attitudes on influenza vaccination in the community.

MATERIAL AND METHODS:

This study was carried out between October-December 2017 in five different community & solidarity centers in Yenimahalle District Municipality in Ankara. The people were invited to take part in the study by a pharmacist and those who are voluntarily agreed to participate and gave a written consent were included. The participants were asked questions about demographics and influenza vaccination.

RESULTS:

A total of 139 people were included (74.8% male) where the mean (±standard deviation) age was 69.3±9.15 year. Of those, 133 (95.7%) participants indicated that they were familiar about influenza vaccination and therefore, further questions were asked on perceptions and attitudes. There were no differences observed between participants vaccinated

and not vaccinated in terms of educational level, monthly income and being alone/living with family (p>0.05). However, vaccinated participants (n=41) are more likely to be older than non-vaccinated (n=92) (mean age: 72 vs 68 years, p= 0.024). Only 38 (27.3%) participants indicated to be vaccinated regularly at each year; the remaining who were not vaccinated regularly each year (n=95) indicated the reasons for not being vaccinated as; not necessary (n=22), inefficacious (n=7), pay no attention (n=6), distrust (n=6), not suggested by a doctor (n=4) and allergy (n=2). Among the participants, 41 (29.5%) indicated to be vaccinated in the last year; of those 29 (71%), 11 (27%), 5 (12%) and 4 (10%) were recommended by physicians, media, pharmacists and friends/relatives, respectively.

CONCLUSIONS:

Despite the fact that public has a common view on influenza vaccination, vaccination rate is still lower than expected. Although demographic features seem not to have an effect on vaccination; prejudices and misunderstanding, lack of information and disinformation and inadequate involvement of healthcare professionals in public health issues may lead to lower rate of vaccination in the community. Therefore, there is a need for active involvement of primary care health professionals in order to increase awareness among public. Pharmacists have opportunity to reach those people in the community and may have influence on misperceptions by provision of information.

ACKNOWLEDGEMENTS:

The authors would like to thank Yenimahalle District Municipality and all participants.

REFERENCES:

1. Ciblak MA (2013). Grip Platformu. Influenza vaccination in Turkey: prevalence of risk groups, current vaccination status, factors influencing vaccine uptake and steps taken to increase vaccination rate. Vaccine. 31(3):518-23.

OP-099: NOVEL TRANSETHOSOME CONTAINING GREEN TEA (CAMELLIA SINENSIS L. KUNTZE) LEAVES EXTRACT FOR ENHANCED SKIN DELIVERY OF EGCG: FORMULATION AND IN VITRO PENETRATION TEST

Effionora A., Delly R., Ghina DA.

Universitas Indonesia, Faculty of Pharmacy, Depok, 164^{2}4, Indonesia

INTRODUCTION:

Green tea (Camellia sinensis L. Kuntze) is one of the plants that widely available with antioxidant activity (1). The major bioactive compounds present in green tea leaves are flavonoids, phenols, that are responsible for antioxidant activities (2). Antioxidant activity in green tea extract depends on the flavonol monomers known as catechins, and epigallocatechin gallate (EGCG). EGCG is the major catechin in green tea which is believed to be the primary source of green tea's beneficial effect (3). Unfortunately, EGCG is hydrophilic in nature and has a low skin penetration and absorption (4). To overcome this problem, transethosome is used as nanolipid vesicle system that can enhance the drug penetration through the skin. Transethosome can be used to entrap the chemical compound or natural ingredients such as EGCG. This study aims to formulate transethosome cream that can enhance the penetration of green tea leaves extract through the skin.

MATERIALS AND METHODS:

Transethosomes were made using thin layer hydration method in three formulations with concentration variation of Span 80 and ethanol. Transethosomes were characterized for morphology using Transmission Electron Microscopy (TEM); particle size, polidispersity index and zeta potential by Particle Size Analizer (PSA); and entrapment efficiency.

RESULTS:

The result showed transethosome F2 containing green tea extract equivalent to 3% EGCG, Lipoid P30 4%, Span 80 0.75% and 30% of ethanol 95% had the best characteristic, which had a spherical shape; particle size 35.35 nm; polidispersity index 0.32; zeta potential -29.97 ± 3.05 mV; and entrapment efficiency 45.26 ± 8.15%. Penetration test of creams was performed using in vitro Franz diffusion cell with the female Sprague Dawley rats skin as a membrane. Transethosome cream had a flux at the first and second phase of 60.56 ± 4.52 and 23.13 ± 1.38 µg.cm-2.hour-1 respectively. Nontransethosome cream had a flux of 25.69 ± 0.83 and 7.36 ± 1.59 µg.cm-2.hour-1 at the first and second phase, respectively.

CONCLUSION:

It can be concluded that transethosome cream could enhance the penetration of EGCG through the skin.

ACKNOWLEDGEMENTS:

All authors acknowledge Universitas Indonesia for support and PITTA Research Grants 2017.

REFERENCES

1. Anand J, Upadhyaya B, Rawat P, Rai N (2015). 3 Biotech, 5 (3), 285-294.
2. Horzic D. Komes D, Belscak A, Ganic KK, Ivekovic D, Karlovic D (2009). Food Chem 115:441–448
3. Fujimura Y, Tachibana H, Maeda YM, Miyase T, Sano M, Yamada K (2002).Journal of Agricultural and Food Chemistry, 50(20), 5729–5734.
4. Patel AR, Velikov KP (2013). Nova Biomedical, Green Tea: Varieties, Production and Health Benefits (pp. 151–166).

OP-100: ALHAGI MAURORUM: A PHARMACEUTICALLY IMPORTANT 'MANNA OR BLESSİNG PLANT' OF SINDH, PAKİSTAN.

Memon, S

National Center of Excellence in Analytical Chemistry, University of Sindh, Jamshoro-Pakistan

INTRODUCTION:

From the advent of civilizations, it came to be known that human being generally depend on plants to cure their illnesses through plants, which in fact are major contributors to the possible source of remedies. Nevertheless, it took time to understand that how to use the plants and their parts before assuming them a blessing. It has been observed that nature has added some toxic matter-with useful bioactive constituents-in plants for their defense mechanism.

MATERIALS AND METHODS:

Herein, a brief but comprehensive emphasis will be given with some aspects concerning foremost pharmaceutical uses of Alhagi Maurorum, an indigenous plant of Sindh, province of Pakistan, followed by discussion about isolation and bioactivity studies of its constituents using with GC-MS.

RESULTS:

It is important that some useful constituents be isolated through separation from plants and used after analyzing and testing their bioactivity, side effects and performing dosage study as well as possible related influencing issues. In this regard, enormous studies have been made on millions of plant species. Many of them have chemically been explored following the studies about their previous uses in traditional medications and focusing on responsible constituents of those bioactivities.

CONCLUSIONS:

In this study, isolation and bioactivitiy studies of constituents of Alhagi Maurorum were done.

REFERENCES:

1. Laghari AH, Memon S, Nelofar A. Khan KM, Yasmin A, Syed MN, Aman A (2010). Journal of Molecular Structures, 965(1-3):65-67.
2. Awaad Amani AS, Maitland DJ, Soliman GA (2006). Pharmaceutical Biology, 44(4):292-296.
3. Laghari AH, Memon S, Nelofar A, Khan KM (2017). Pakistan Journal of Scientific and Industrial Research. 60 (2): 59-66.
4. Demir E, Laghari AH, Sökmen M, Memon S (2015). Separation Science Techniques. 50 (4) 529-535

OP-101: CLIPS (CHEMICAL LINKAGE OF PEPTIDES ONTO SCAFFOLDS) TECHNOLOGY APPLIED TO OPIOID PEPTIDES RESEARCH

Mollica A.

Dipartimento di Farmacia, Università di Chieti-Pescara "G. D'Annunzio", Chieti, Italy

INTRODUCTION:

CLIPS (Chemical LInkage of Peptides onto Scaffolds) technology [1] is a novel and still unexplored versatile method for constraining and functionalizing the 3D-conformation of peptides.

MATERIALS AND METHODS:

This novel cyclization type involves the cyclization of linear peptides via reaction with a small scaffold like dibromoxylenes. The bromine anchor points react exclusively with the thiols of the Cys or Pen in the peptide and attach to the peptide via multiple thio-ether bonds.

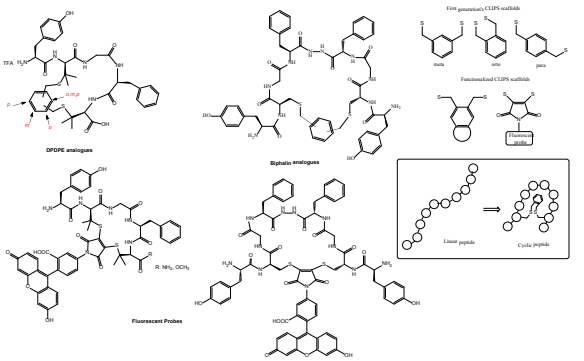


Figure 1. CLIPS Scaffolds.

RESULTS:

Six cyclic analogues of DPDPE, biphalin and three fluorescent probes were prepared and characterized as m/d-opioid receptors agonists.[2,3]

CONCLUSIONS:

The novel biphalin and DPDPE derivatives were tested by in vitro and by in vivo animal model of pains showing higher potency and efficacy than the parent compounds..

REFERENCES:

1. Stefanucci A et al. (2017). ACS Med. Chem. Lett. 2017, asap.
2. Stefanucci A et al. (2017). ACS Med. Chem. Lett., 8:449–454.
3. Stefanucci A et al. (2017). Future Medicinal Chemistry, 9.

OP-102: BIOASSAY-GUIDED ISOLATION AND IDENTIFICATION OF ANTI INFLAMMATORY SESQUITERPENE LACTONES FROM CHRYSOPHTHALMUM MONTANUM (DC.) BOISS

[1] Ayaz, F., [2] Kupeli Akkol, E., [3,4] Goren, N., [5] Calis, I., [2] Guragac F.T., [6] Duman, H., [4] Choudhary, M.I., [2] Kucukboyaci, N.

[1]Selcuk University, Department of Pharmacognosy, Konya, Turkey

[2]Gazi University, Department of Pharmacognosy, Ankara, Turkey

[3]Yildiz Technical University, Department of Molecular Biology and Genetics, İstanbul, Turkey

4University of Karachi, International Center for Chemical Sciences, Karachi, Pakistan

5Near East University, Department of Pharmacognosy, Nicosia, Turkish Republic of Northern Cyprus

6Gazi University, Department of Biology, Ankara, Turkey

INTRODUCTION:

Asteraceae family is well-known as a good source of sesquiterpene lactones (SLs) responsible for different biological activities. The genus Chrysophthalmum Schultz. Bip (Asteraceae) is represented by four species worldwide. Among them, C. montanum (DC.) Boiss. is distributed Turkey, the North of Iraq and Syria (1). C. montanum, commonly called “tutça” or “nezle otu”, is a herbaceous perennial herb growing in the rock crevices and limestone cliffs of the Eastern region of Turkey. In Turkish folk medicine it is used to treat eye diseases, sinusitis, flu and other inflammatory respiratory diseases as well as for wound healing (2). In the light of this information, we aimed to isolate and evaluate the potential anti-inflammatory compounds from the aerial parts of C. montanum.

MATERIALS AND METHODS:

The anti-inflammatory activity of C. montanum aerial parts, carrageenan- and PGE2-induced hind paw edema, and acetic acid-induced increase in capillary permeability models were used on mice. The methanol extract of the plant was first fractionated into four subextracts; namely, n-hexane, chloroform, n-butanol, and remaining aqueous subextracts. Among them, the CHCl3 subextract exhibited the most potent anti-inflammatory activity and was thus subjected to bioassay-guided fractionation and isolation procedures.

RESULTS:

Four known guaianolide type sesquiterpene lactones, 6α-acetoxy-4α-hydroxy-1βH-guaia-9.11(13)-dien-12.8α-olide (1), 6α-acetoxy-4α-hydroxy-9β.10β-epoxy-1βH-guaia-11(13)-en-12.8α-olide (2), 4α,6α-dihydroxy-1β,5α,7αH-guaia-9(10),11(13)-dien-12,8α-olide (3), and (4α,5α,8β,10β)-4,10-dihydroxy-1,11(13)-guaidien-12,8-olide (4) were isolated from the CHCl3 subextract. The structures of the isolated compounds were elucidated by means of spectroscopic techniques (UV, IR, 1D and 2D NMR, and EI-MS and HREI-MS). The methanol extract, CHCl3 subextract and compounds 3 and 4 were shown to possess anti-inflammatory activity on mentioned in vivo models at 100 mg/kg dose. The rest of the subextracts and isolated sesquiterpene lactones displayed to be inactive in all of the assays.

CONCLUSIONS:

The results provide a biological and phytochemical basis for the traditional use of C. montanum for the inflammatory diseases in Turkish folk medicine.

ACKNOWLEDGEMENTS:

This study was supported by Gazi University Research Foundation [grant number 02/2017-11].

REFERENCES:

1. Grierson AJC (1975). In: Davis PH (ed). Chrysophthalmum Schultz Bip. Flora of Turkey and the East Aegean Islands (Vol. 5). Edinburgh University Press, Edinburgh, pp 52-53.
2. Arasan S, Kaya I (2015). Journal of Food and Nutrition Research, 3(5): 337-340.

OP-103: OPTIMIZATION THE PREPARATION PROCESS OF METHOTREXATE LOADED HUMAN SERUM ALBUMIN NANOPARTICLES

Ilem Ozdemir, D., Ekinci, M., Ozgenc, E., Gundogdu, E., Asikoglu, M.

Ege University, Faculty of Pharmacy, Department of Radiopharmacy, Izmir, Turkey

INTRODUCTION:

Methotrexate (MTX) is a most widely used anticancer drug. However, the clinical application of MTX is limited by side effects and drug resistance. Nanoparticulate delivery systems containing anticancer drugs have been continued to develop due to their tumor-targeting abilities (1). Human serum albumin (HSA) based nanoparticulate systems are play an important role because of the ideal properties such as being non-toxic, non-antigenic, having active targeting ability (2, 3). The objective of the present study is the optimization of the preparation process of MTX loaded HSA nanoparticles (NPs).

MATERIALS AND METHODS:

HSA-NPs were prepared by small modification on the desolvation technique as described previously (2)in particular for the in vivo behaviour of nanoparticles after intravenous injection. The objective of the present study is the development of a desolvation procedure for the preparation of HSA-based nanoparticles under the aspect of a controllable

particle size between 100 and 300nm in combination with a narrow size distribution. A pump-controlled preparation method was established which enabled particle preparation under defined conditions. Several factors of the preparation process, such as the rate of addition of the desolvating agent, the pH value and the ionic composition of the HSA solution, the protein concentration, and the conditions of particle purification were evaluated. The pH value of the HSA solution prior to the desolvation procedure was identified as the major factor determining particle size. Varying this parameter, (mean. Different drug concentrations were examined to achieve ideal properties of NPs. In principle, HSA and 0.5-15 mg MTX dissolved in 10 mM NaCl solution under constant stirring for 2 h. Desolvating agent was added drop wisely. Particle crosslinking was induced by addition of 8% glutaraldehyde in water under stirring of the suspension over a time period of 24 h. After incubation of crosslinking process, the resulting NPs were purified by two cycles of centrifugation. The supernatants were collected and the concentration of free MTX was analyzed by High Performance Liquid Chromatography (HPLC) for the encapsulation efficiency (EE). Particle size, polydispersity index (PDI) and zeta potential value of MTX-HSA-NPs were measured by a Zetasizer Nano ZS.

RESULTS:

According to HPLC study results, the EE of MTX-HSA-NPs was found over 80%. The average particle size, PDI and zeta potential of ideal MTX-HSA-NP formulation were found as 365.9±54.39 nm, 0.370±0.092 and -39.0±1.33 mV, respectively.

CONCLUSIONS:

NPs with incorporated MTX were prepared by incubation the drug with matrix protein prior to the desolvation and crosslinking process. The characteristics of NPs were found to be depend on the concentration of MTX. The ideal NPs were obtained at MTX concentration 1 mg with 150 mg of HSA.

ACKNOWLEDGEMENTS:

This study was supported by Ege University, Scientific Research Project Comission (16-ECZ-016) and Aliye Uster Foundation. Also, the authors would like to thank to TUBITAK (108S083) and T.R. Prime Ministry State Planning Organization Foundation (09-DPT-001).

REFERENCES:

1. 1. Bae S et al., (2012). Biomaterials, 33(5):1536–46.
2. 2. Langer K et al., (2003). International Journal of Pharmaceutics, 257(1–2):169–80.
3. 3. Langer K et al., (2008). International Journal of Pharmaceutics, 347(1–2):109–17.

OP-104: BIOMASS AS A SOURCE OF MICROCRISTALLINE CELLULOSE – CHEMICAL AND TECHNOLOGICAL CHARACTERIZATION

[1] Bakic, T., [2] Krstic, M., [3] Maksimovic, Z., [1] Razic, S.

[1]University of Belgrade, Faculty of Pharmacy, Department of Analytical Chemistry, Belgrade, Serbia

[2]University of Belgrade, Faculty of Pharmacy, Department of Pharmaceutical Technology and Cosmetology, Belgrade, Serbia

[3]University of Belgrade , Faculty of Pharmacy, Department of.Pharmacognosy, Belgrade, Serbia

INTRODUCTION:

It has been estimated that as much as 140 billion metric tons of biomass is generated every year from agriculture worldwide. Serbia's annual production is about 12.5 million tons of biomass, where over 50% lie in corn biomass. Widely available, renewable, and virtually free, waste biomass has already become an interesting and important potential source for microcrystalline cellulose (MCC). This work was focused on extraction and characterization of microcrystalline cellulose from agricultural biomass and testing it as potential excipients in the pharmaceutical industry.

MATERIALS AND METHODS:

Samples: agricultural waste (corn) collected in Belgrade. Isolation: extraction with hexane and methanol, delignification, bleaching, hydrolysis, rinsing and drying. Identification and chemical characterization: Infrared Spectroscopy with Fourier transformation (FTIR), Scanning Electron Microscopy (SEM), Inductively coupled plasma atomic emission spectrometry (ICP-AAE) and Ionic chromatography (IC).

Pharmaceutical-technological tests: flow, bulk and taped density, Carr's index and Hausner's ratio, determination of true density, simulation of material compaction using Gamlen Tableting D series, determination of compatibility and compressibility, disintegration and tablet's dissolution rate. All results were compared with commercially available microcrystalline cellulose (Vivapur®).

RESULTS:

Microcrystalline cellulose was successfully isolated from lignocellulosic biomass (corn). The obtained MCC showed excellent features in terms of safety, physical-chemical and pharmaceutical-technological properties, as well.

CONCLUSIONS:

The results of this work indicate that corn has a high potential as a source of MCC with satisfactory characteristics, with perspective of implementing the methodology presented in this work on a large scale

production.

ACKNOWLEDGEMENTS:

This study was supported by by the projects No. TR 34007, OI 173021 and III43009, supported by the Ministry of Education, Science and Technological Development, Republic of Serbia.

REFERENCES:

1. US EPA Method 3015A. 2007
2. Gamlen M, Dey D (2014). Biocity Nottingham, pp 3
3. Vanhatalo KM, Parviainen KE, Dahl OP (2014). Bioresources, 9(3):4741

OP-105: STUDIES ON ANTIFUNGAL KETOXIMES

Karaburun, AC.

Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskisehir, Turkey

INTRODUCTION:

World Health Organisation (WHO) considers antimicrobial resistance as a complex problem that affects all of society and is driven by many interconnected factors. Greater innovation and investment are required in research and development of new antimicrobial medicines, vaccines, and diagnostic tools. Particularly, in fungus infections the problem is more complexed hence, biochemical similarity of the human cell and fungi forms is a handicap for selective activity. As part of the efforts of finding novel antifungals, studies on oxime moiety bearing compounds is of interest. Notable antifungal results obtained from the oximes in these works (1-3). One of the aryl/alkyl residues of ketoxime was replaced with benzofuran and obtained significant antifungal activity, against Candida albicans, from previous works referred above. In a 3-D molecular modelling study of aryl benzofuran-2-yl ketoxime derivatives as Candida albicans N-myristoyl transferase inhibitors, among some other quantitative structure activity relationship and molecular docking data, it was reported that the lipophilic interaction between phenyl of benzofuran core is important for antifungal activity (4). In light of these findings, chlorinated derivatives of those mentioned ketoximes aimed.

MATERIALS AND METHODS:

Previously reported procedures (1-3) were used for the synthesis of the aimed molecules.

RESULTS:

The structure elucidation of the compounds was performed by IR, 1H-NMR and mass spectroscopic data and elemental analyses results. Antifungal activities of the compounds were examined.

CONCLUSIONS:

The compounds were successfully obtained and elucidated as ketoximes, oxime ethers and esters of chlorobenzofuran aryl ketones. They showed moderate antifungal activity as expected.

REFERENCES:

1. Demirayak et al., (2002). Farmaco, 57:609-612.
2. Benkli et al., (2003). Arch. Pharm.Res., 26:202-206.
3. Gundogdu Karaburun et al., (2006). Eur. J. Med. Chem., 41:651–656.
4. Telvekar et al., (2008). QSAR Comb. Sci., 27:1193-1203.

OP-106: THERAPEUTIC EFFICIENCY OF CICHORIUM INTYBUS L. IN A RAT MODEL OF SURGICALLY-INDUCED ENDOMETRIOSIS BY AUTO-TRANSPLANTATION OF UTERINE TISSUE

[1,2,3] Ilhan, M., [2] Ali Z., [2] Khan, IA.,[1] Kupeli Akkol E.

[1]Gazi University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

[2]University of Mississippi, School of Pharmacy, National Center for Natural Products Research, USA

[3]Yuzuncu Yıl University, Faculty of Pharmacy, Department of Pharmacognosy, Van, Turkey

INTRODUCTION:

The leaves of Cichorium intybus L. are used for treating of menopausal symptoms and the roots are used against menstrual diseases, and also the all plant is used for the uterine diseases and infections (1-4).

MATERIALS AND METHODS:

The aerial parts of C. intybus were extracted with n-hexane, ethyl acetate and methanol, successively. To evaluate efficacy potential of the extracts and fractions from C. intybus, surgically-induced endometriosis rat model was used. In this model, adhesion scores of endometriotic implant, endometriotic implant volumes, and the cytokine levels of peritoneal fluids were evaluated. After biological activity studies, phytochemical analyses were performed on the active extract and the fractions obtained from the active extract.

RESULTS:

According to the results, the methanol (MeOH) extract significantly decreased the adhesion scores, endometriotic implant volumes, and the cytokine levels of peritoneal fluids. Following the biological activity studies, the MeOH extract was applied to RP-18 column to get four main fractions (Frs. A-D). The efficacies of those fractions were evaluated again to exhibit the compound/s responsible for

the activity. At the end of the biological activity experiments, Frs. B and C showed significant activity compared to the control group. 6,8,11-Epi-desacetylmatricarin, cichorioside B, and two new sesquiterpene lactones namely (((3R,3aR,4S,9bR)-4-hydroxy-9-(hydroxymethyl)-6-methyl-2,7-dioxo-2,3,3a,4,5,7,9a,9bocta hydroazuleno[4,5-b] furan-3-yl)methyl)proline,(((3R,3aR,4S,9bR)-4-hydroxy-6,9-dimethyl-2,7-dioxo-2,3,3a,4,5,7,9a,9b-octahydroazuleno[4,5-b]furan-3-yl)methyl)proline were isolated from Fr. B. Quercetin 3-O-β-D-glucuronide, quercetin 3-O-β-D-glucoside, kaempferol 3-O-β-D-glucoside were isolated from Fr. C.

CONCLUSIONS:

As a conclusion, the MeOH extract could be used for treating endometriosis due to its sesquiterpene lactones and flavonoids. In this study, two new sesquiterpene lactones were isolated from the aerial parts of C. intybus.

ACKNOWLEDGEMENTS:

This study was supported by 2214/A-International Doctoral Research Fellowship Programme, provided by "The Scientific and Technological Research Council of Turkey (TUBITAK)"

REFERENCES:

1. Estévez MA, Báez F (1998). Plantas Curativas: Usos Populares y Cientificos. Caribe Soy, Santo Domingo, Dominican Republic.
2. Kapahi et al., (1993). Ancient Science of Life, 13:119-124.
3. Ososki et al., (2002). Journal of Ethnopharmacology, 79:285-298.
4. Gumus I (1994). Turkish Journal of Botany, 18:107-112.

OP-107: SYNTHESIS OF NOVEL CONDENSED 1,4-DIHYDROPYRIDINE DERIVATIVES AND THEIR BINDING MECHANISM TO L-TYPE CALCIUM CHANNEL

[1] Gunduz, MG., [2] Schaller, D., [3] Zhang, FX., [3] Zamponi, GW.,[2] Wolber, G.

[1] Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

[2] Freie Universität, Institute of Pharmacy, Department of Pharmaceutical and Medicinal Chemistry, Berlin, Germany

[3] University of Calgary, Hotchkiss Brain Institute and Alberta Children's Hospital Research Institute,Department of Physiology and Pharmacology, Calgary, Canada

INTRODUCTION:

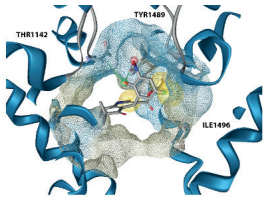
Although dihydropyridines (DHP) like nifedipine and isradipine have been successfully used as anti-hypertensive drugs for decades, the detailed structure activity relationships between DHPs and their interaction sites within the DHP binding pocket of the L-type calcium channel (Cav1.2) are still incompletely understood (1). In this study, we aimed at rationalizing the binding mode of DHPs to Cav1.2 and explaining the structure activity relationship of a DHP compound class with a condensed ring system.

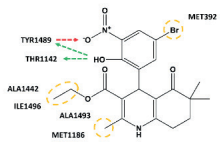
MATERIALS AND METHODS:

A homology model was created based on the recently released crystal structure of the closely related calcium channel Cav1.1 (2). Twenty two novel DHPs with a condensed ring system were synthetized according to a modified Hantzsch reaction and tested in-vitro using whole-cell patch clamp technique for ability to block Cav1.2 to challenge our binding hypothesis.

RESULTS:

Patch clamp assays revealed two novel compounds with comparable activity to our reference molecules. Docking studies were performed on developed homology model of Cav1.2 to gain insights into the binding modes. Poses were analyzed to support the results of the structure activity relationship analysis discussed before. Identified binding poses of the compounds were subjected to an unrestrained molecular dynamics simulation and the compounds stayed stable at their binding sites over the whole simulation time.





CONCLUSIONS:

In this study, 22 novel DHPs were synthetized and tested for effective inhibition of Cav1.2. We aimed at rationalizing the binding mode of DHPs with special focus on derivatives with a condensed ring system. We identified a binding mode for nifedipine, isradipine and our active 1,4-DHP analogs to Cav1.2 that is also able to explain the structure activity relationships.

ACKNOWLEDGEMENTS:

The authors acknowledge the financial support provided by Scientific Research Fund of Hacettepe University, Turkey through Project THD-2016-10016.

REFERENCES:

1. Zamponi GW, Striessnig J, Koschak A, Dolphin AC (2015). Pharmacological Reviews, 67:821-870.
2. Tang L, Gamal El-Din TM, Swanson TM, Pryde DC, Scheuer T, Zheng N, Catterall WA (2016). Nature, 537(7618):117-121.

OP-108:WOUND HEALING EFFECTS OF SALVIA HYPARGEIA ETHANOL EXTRACTS ON EXCISIONAL AND INCISIONAL WOUND MODELS IN DIABETIC RATS

[1] Ozay, Y., [2] Guzel, S., [3] Gokalp Ozkorkmaz, E., [4] Kumas, M., [5] Uzun, C., [6] Yildirim, Z.

[1]Adiyaman University, Faculty of Medicine, Department of Medical Biology, Adiyaman, Turkey

[2]Mersin University, Faculty of Pharmacy, Department of Pharmacognosy, Mersin, Turkey

[3]Ankara Yildirim Beyazit University, Faculty of Health Sciences, Ankara, Turkey

4Bezmi Alem Vakif University, Faculty of Medicine, Department of Histology, Istanbul, Turkey

5Mersin University, Faculty of Medicine, Department of Biophysics, Mersin, Turkey

6Etimesgut Public Health Laboratory, Etimesgut, Ankara, Turkey

INTRODUCTION:

Diabetes mellitus is a well known disease causing hyperglycemia, impaired homeostatic process, inhibition of inflammatory response, generation of reactive oxygen species (1) with reduction in collagen production, differentiation of the extracellular matrix and fibroplasia (2). A wide variety of medicinal plants for wound healing in diabetes can be found in literature and widely used in folk medicine (3). The aim of this study was to indicate the effects of ointment prepared with Salvia hypargeia, an endemic plant from Turkey, on diabetic wounds.

MATERIALS AND METHODS:

Male Wistar albino rats were used in this study (n:60), divided into 5 groups. A single dose of 45 mg/dl streptozotocin was given to rats (i.p.) to introduce diabetes. Excisional and incisional wounds were created under anesthesia. Ethanol extracts of 0.5% and 1% of S. hypargeia were added respectively in mixtures to prepare the simple ointment and were topically applied to wounds. Tissues were evaluated with macroscopic, histopathological and biochemical analysis.

RESULTS:

Wound healing ratios of 0.5% S. hypargeia group (63.4 ±7.7&99,3±1,6) and 1% S. hypargeia group (65.5±12.3&99.9±0.01) were statistically significant (P<0.01) compared to diabetic control group (35.9±22.8&75.1±18.8) in excisional skin wounds on the 7th and 14th days. Also healing ratios in incisional skin wounds of 0.5% (78.1±7.4&98.5±2.2) and 1% S. hypargeia groups (84.4±15.9&99.4±0.8) were statistically significant (P<0.01) compared to diabetic control group (30.5 ±17.1&72.9±10.8) on the 7th and 14th days. Hydroxyproline (0.31±0.3&0.34±0.2) and GSH(10.7±3.1&7.6±0.9) levels of 0.5%and 1%S. hypargeia groups were statistically significant (P<0.01) on the 14th day. Histopathological results revealed reepithelialization and formation of granulation tissue in all S. hypargeia groups as well.

CONCLUSIONS:

In conclusion, ointment prepared with extract of Salvia hypargeia has a healing effect on excisional and incisional diabetic wounds.

ACKNOWLEDGEMENTS:

This study was supported from Adiyaman University Scientific Research Center TIPFBAP/2015-0004.

REFERENCES:

1. American Diabetes Association (2016). Diabetes Care, 39: 54–55.
2. Tracy L, Minasian RA, Caterson EJ (2016). Advances In Wound Care, 5: 119-136.
3. Suntar I, Akkol EK, Senol FS, Keles H, Erdogan Orhana I (2011). Journal of Ethnopharmacology, 135:71-77.

OP-109: THE 5-HYDROXYTRIPTAMINE 2A RECEPTOR -1438A/G AND 102T/C POLIMORPHISMS AND NAUSEA SIDE EFFECT IN CITALOPRAM TREATED MAJOR DEPRESSIVE DISORDER PATIENTS

[1] Demirbugen, M., [2] Uckun, Z., [1] Yuce Artun N., [3] Devrimci Ozguven, H., [1] Suzen, HS.

[1] Ankara University, Department of Pharmaceutical Toxicology, Ankara, Turkey

[2] Mersin University, Department of Pharmaceutical Toxicology, Mersin, Turkey

[3] Ankara University, Department of Psychiatry, Ankara, Turkey

INTRODUCTION:

Major depressive disorder (MDD) is the most common mental disorder all around the world and today approximately 350 million people suffer from MDD. Citalopram is a widely prescribed agent of SSRIs[1]. Despite, SSRIs are associated with less adverse drug reactions, nausea and vomiting is observed approximately 40% of the MDD patients [2]. There are different mechanisms and factors for the occurrence of nausea and vomiting. Serotonine receptor polymorphisms might be one of these factors, which contribute nausea and vomiting. Our aim was to evaluate the associations between the Serotonine-2A receptor (HTR2A) gene 102T/C and -1438A/G single nucleotide polymorphism and nausea in citalopram treated patients.

MATERIALS AND METHODS:

Genomic DNA was isolated from 63 MDD patients who were treated with daily CIT. The HTR2A 102T/C and -1438A/G polymorphisms analyzed by using

PCR-RFLP techniques.

RESULTS:

We have found that, in the patients treated with CIT, there was a significant difference in the genotypic distribution associated with -1438A/G polymorphism between patients with and without nausea (X2=6.894, p=0.032). Moreover, logistic regression analysis revealed a significant association between nausea/vomiting side effect and -1438A/G polymorphism. That is patients with the G allele were at a higher risk for developing nausea/vomiting (p=0.030, OR=2.469). The 102T/C polymorphism in the HTR2A gene had no significant effect on the nausea/vomiting side effect among participants.

CONCLUSIONS:

The present study demonstrates that the HTR2A gene -1438A/G polymorphism might be associated with nausea/vomiting side effect in patients who were treated with CIT.

ACKNOWLEDGEMENTS:

This study was supported by Research Fund of Ankara University, Ankara, Turkey (Project17H0237003)

REFERENCES:

1. Organization, W.H. Depression: A global Crisis. 2012 [cited 2018 29 March]; Available from: http://www.who.int/mental_health/management/depression/wfmh_paper_depression_wmhd_2012.pdf.
2. Suzuki Y, Sawamura K, et al., (2006). Polymorphisms in the 5-hydroxytryptamine 2A receptor and CytochromeP4502D6 genes synergistically predict fluvoxamine-induced side effects in japanese depressed patients. Neuropsychopharmacology,. **31**(4): p. 825-31.

OP-110: SYNTHESIS AND EVALUATION OF BENZIMIDAZOLE AND 2-PYRAZOLINE DERIVATIVES AS MULTI-TARGET-DIRECTED LIGANDS AGAINST ALZHEIMER'S DISEASE

[1] Ozadali Sari, K., [2] Tuylu Kucukkilinc, T., [2] Ayazgok, B., [1] Balkan, A., [1] Unsal Tan, O.

[1] Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

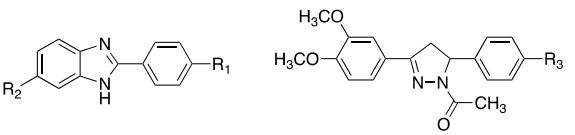
[2] Hacettepe University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey

INTRODUCTION:

Alzheimer's disease (AD) is a multifactorial complex neurodegenerative disorder and apparently involves several different cellular and molecular processes. However the main therapeutic strategy today is the use of acetylcholinesterase (AChE) inhibitors; the elevation of butyrylcholinesterase (BChE) levels, the accumulation of Aβ peptides, tau protein phosphorylation, neuroinflammation of the central nervous system are the other important factors in the pathogenesis of the disease (1,2). Multifactorial nature of AD with complex pathological mechanisms fits well with Multi Target Directed Ligand (MTDL) development strategy (3). Considering this strategy, the study is focused on synthesis and biological evaluation of some new benzimidazoles and 2-pyrazolines to obtain novel MTDLs by combining BChE and Aβ aggregation inhibitory activities in one neuroprotective structure.

MATERIALS AND METHODS:

The structures of the synthesized compounds were elucidated by spectral and elemental analysis data. Inhibitory effects of the compounds on AChE/BChE enzymes and fibril formation were evaluated by using Ellman's method and fluorimetric methods in respectively. Further, H2O2- and Aβ1–40-induced cytotoxicity tests were performed to evaluate the neuroprotective effects of the compounds. The binding mode of the the compounds in the active site of the cholinesterase enzymes were tried to identify by molecular modeling studies.



RESULTS:

Among the benzimidazole derivatives, Compound 12 (IC50 BChE: 5.18±1.22 μM, SI: 6.7) showed the highest inhibitory activity on BChE. Compound 20, a member of 2-pyrazoline series, selectively inhibited (IC50 BChE: 0,34 μM, SI: 114,2) BChE. H2O2 and Aβ1-40 induced cytotoxicity studies showed that the most of the compounds possessed neuroprotective feature by increasing cell viability (compared to control).

CONCLUSIONS:

All these results suggested that some of benzimidazole and 2-pyrazoline derivatives could be a promising multi-target lead candidate against AD.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-114S374)

REFERENCES:

1. Anand P, Singh B (2013). Arch Pharm Res 36:375–399
2. Taylor et al. (2002). Science 296:1991–1995
3. Agis-Torres et al. (2014). Curr Neuropharmacol 12:2-36

OP-111: BISMUTH OXIDE NANOPARTICLES CAUSED NEUROTOXICITY VIA OXIDATIVE STRESS IN VITRO.

Oztas, E., Aykanat, B., Can, Z., Baram, E., Ozhan, G.

Istanbul University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Beyazit, 34116, Istanbul, Turkey

INTRODUCTION:

Nanotechnology Consumer Products Inventory listed over 500 consumer products contains metals and metal oxides (1). Bismuth based nanoparticles have attracted the attention especially in biological sciences and commonly used in medical applications. By our group, the bismuth oxide nanoparticles (Bi2O3-NPs) were reported to induce oxidative stress and cause apoptosis and DNA damage in several mammalian cell lines including HepG2, NRK-52E, Caco-2 and A549 (2). Therefore, in the present study, we aimed to assess the neurotoxic potential and possible toxicity mechanisms of Bi2O3-NPs in SH-SY5Y cells.

MATERIALS AND METHODS:

Cytotoxic activities of the Bi2O3-NPs were determined by MTT and LDH assays. ROS production was determined by flow cytometry using H2DCFDA and GSH, CAT and SOD levels were measured by ELISA. The mRNA expression levels of inflammation related genes were determined using LightCycler 480 Probes Master and Catalog Assays on the Roche RealTime LightCycler 480 II platform.

RESULTS:

$Bi2O^3$-NPs decreased the cell viability through disruption on mitochondrial activity (IC50: 77.57 µg/mL) and membrane integrity (IC50: 16.97 µg/mL) which are determined using MTT and LDH assays, respectively. At 50 µg/mL of $Bi2O^3$-NPs, ROS production significantly induced as well as,the levels of CAT and SOD. In immune response, mRNA expression levels of IL-6 were increased more than 1.5-fold in all doses; whereas, MAPK8, NF-κB and TNF-α expressions were remained unchanged.

CONCLUSIONS:

Bi2O3-NPs induced inflammation-related oxidative stress via activation of pro-inflammatory cytokine, IL-6. It should raise concern about the safety associated with their applications in consumer products according to the obtained results and the mentioned literature. Also, supporting studies in vivo are needed to fully understand the toxicity mechanism of Bi2O3 nanoparticle.

ACKNOWLEDGEMENTS:

This work was conducted as “Final Project” of Pharmacy students namely Aykanat B, Can Z. and Baram E., and, funded by the Research Fund of Istanbul University (Project No. TLO-2017-27472). Oztas E. (Supervisor) and Ozhan G. (Promoter) thank to undergraduate students for their great effort and commitment.

REFERENCES

1. Vance ME, Kuiken T, et al., (2015). Nanotechnology in the real world: Redeveloping the nanomaterial consumer products inventory. Beilstein Journal of Nanotechnology, 6, 1769.
2. Abudayyak M, Oztas E, et al., (2017). Investigation of the toxicity of bismuth oxide nanoparticles in various cell lines. Chemosphere, 169, 117-123.

OP-112: ENUMERATION OF ESCHERICHIA COLI BASED ON SERS TECHNIQUE IN A PASSIVE TYPE MICROFLUIDIC CHIP

[1] Dogan, U., [1] Kasap, EN., [2] Çogun, F., [2] Yildirim, E., [3] Cetin, D., [4] Suludere, Z., [5,6] Boyaci, IH., [1] Ertas, N., [1] Tamer, U.

[1]Gazi University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

[2]Cankaya University, Faculty of Engineering, Department of Mechanical Engineering, Ankara, Turkey

[3]Gazi University, Gazi Faculty of Education, Department of Mathematics and Science Education, Ankara, Turkey

4Gazi University, Faculty of Science, Department of Biology, Ankara, Turkey

5Hacettepe University, Department of Food Engineering, Ankara, Turkey

6Hacettepe University, Food Research Center, Ankara, Turkey

INTRODUCTION:

Microorganism detection and quantification is a vital research area for human being in diagnosis, medicine, pharmacy, food industry etc. (1). Classical colony counting methods needs at least 12-48 hours to give a reliable result which is very time consuming especially when fast result is crucial. In the present study, rapid, sensitive and specific biosensor have been developed by using modified magnetic nanoparticles and modified gold nanorods tagged with a Raman reporter molecule to enumerate Escherichia coli (E.coli).

MATERIALS AND METHODS:

Iron oxide core gold shell magnetic nanoparticles (MNPs) were synthesized and modified with biotinylated antibodies specific to E.coli. Similarly, gold nanorods were synthesized and modified with a Raman label and biotinylated E.coli antibodies. Modified nanoparticles were interacted with E.coli solutions which have different initial bacteria concentrations and SERS measurements were taken (Fig. 1).

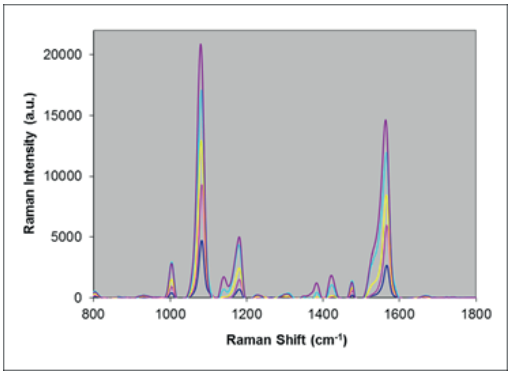


Figure 1. SERS signals obtained from E. coli solutions (101–105 cfu/mL)

RESULTS:

Our results showed that modified MNPs and gold nanorods were successfully conjugated with E. coli. The developed method could detect 101–105 cfu/mL of E. coli in 1h, reliably. A linear relationship of the Raman peak intensity and logarithmic bacteria concentrations was observed in calibration graph. Selectivity of the method was also examined by taking SERS measurements for Enterobacter dissolvens (E. dissolvens), and Staphylococcus aureus (S. aureus) by utilizing the same procedure, and no significant interference was observed.

CONCLUSIONS:

A fast, sensitive and selective biosensor system was developed and applied to spiked milk samples to show the applicability of this biosensor to real samples with a total analysis time less than 60 minutes, successfully. Furthermore, many other samples like urine, contaminated water and food products etc. can be examined by using this developed biosensor system due to its significant advantages.

ACKNOWLEDGEMENTS:

This work was supported by a grant of TUBITAK (Project No: 114Z408)

REFERENCES:

1. Luo PG, Stutzenberger FJ (2008). Adv. Appl. Microbiol., 63:145-181.

OP-113: SYNTHESIS AND CHOLINESTERASE INHIBITORY POTENTIAL OF SOME PYRIDINIUM-3-CARBOHYDRAZIDE-HYDRAZONE DERIVATIVES

Parlar, S.

Ege University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Izmir, Turkey

INTRODUCTION:

Inhibition of acetylcholinesterase (AChE) enyzme is the therapeutic target of drugs designed to manage various disorders such as myasthenia gravis, glaucoma, Lewy body dementia, and Alzheimer's disease (1). AChE inhibitors are used for the treatment of these disorders, which improve cholinergic functions by elevating acetylcholine (ACh) levels in cholinergic synapses. AChE is the primary enzyme responsible for the degradation of ACh, while butyrylcholinesterase (BuChE) plays a secondary role (2). Pyridostigmine, a reversible AChE inhibitor used for the treatment of myasthenia gravis, includes a quaternary pyridinium-carbamate moiety in the molecule structure. Based on the AChE protein structure, this cationic nitrogen atom plays an important role in enzyme-ligand interactions (3). Within this contex, in this study, pyridinium moiety was chosen as a core structure and a series of quaternary pyridiniumhydrazide-hydrazone derivatives were designed to synthesize as potential anti-ChE inhibitors (Fig 1).

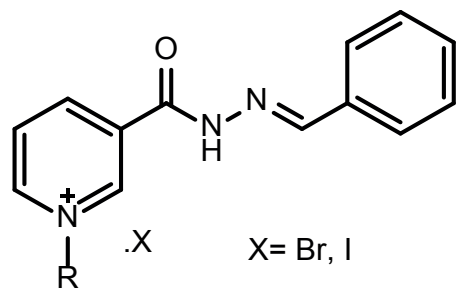


Fig. 1. The structure of the synthesized compounds

MATERIALS AND METHODS:

The final compounds were synthesized according to the reported method (4). Their AChE and BuChE inhibitory activities were assayed using the method of Ellman et al (5).

RESULTS:

In the present study, a series of pyridiniumhydrazide-hydrazone derivatives were synthesized and evaluated for their anti-ChE activities. Chemical structures of the synthesized compounds were confirmed by spectral IR, 1H NMR, and ESI-MS analysis. According to the biological activity results, the compounds were found to have inhibitory potential in different ratios against AChE/BuChE.

CONCLUSION:

The obtained activity results suggested that these pyridiniumhydrazide-hydrazone derivatives might be promising leads for the development of anti-ChE drugs.

REFERENCES:

1. Khan et al., (2007). Journal of Enzyme Inhibition and Medicinal Chemistry, 22:722-725.
2. Zacks S, Blumberg J (1961). Journal of Histochemistry and Cytochemistry, 9:317-324.
3. Refolo LM, Fillit HM (2004). Journal of Molecular Neuroscience, 24:1-8.
4. Hassan et al., (2009). Bioorganic & Medicinal Chemistry, 17:1681-1692.
5. Ellman et al., (1961). Biochemical Pharmacology, 7:88-95.

OP-114:THE EFFECTS OF BISPHENOL A AND/OR MONO(2ETHYLHEXYL)PHTHALATE ON CYTOTOXICITY AND ENDOPLASMIC RETICULUM STRESS IN HUMAN HEPATOMA CELL LINE

[1,2] Ozkemahli, G., [3] Ercan, A., [1] Erkekoglu, P., [1,4] Kocer Gumusel, B.

[1]Hacettepe University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

[2]Erzincan University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

[3]Hacettepe University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey

4Lokman Hekim University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

INTRODUCTION:

Bisphenol A (BPA) is used primarily for production of polycarbonate plastics. Di(2-ethylhexyl) phthalate (DEHP) is used in the manufacturing of polyvinylchloride (PVC). They are suggested to act as peroxisome proliferators and exert hepatotoxicity. Mono (2-ethylhexyl)phthalate is the main metabolite of DEHP. MEHP is even more toxic than the parent compound. However, combined effects of these chemicals are not well-studied. Endoplasmic reticulum (ER) functions to fold and process secreted and transmembrane proteins. Environmental and genetic factors that disrupt ER function can lead to the accumulation of misfolded/unfolded proteins in the ER lumen. This phenomenon is called “ER stress”. A signaling network called the “Unfolded Protein Response (UPR)” is activated after ER stress is induced. UPR usually restores ER homeostasis, and later promotes cell survival. However, under unresolvable ER stress conditions, the UPR promotes apoptosis. Many environmental chemicals can induce ER stress and finally apoptotic cell death. The aim of this study was to determine cytotoxicity and ER stress caused by BPA and/or MEHP exposure in human hepatoma cell line (HepG2 cells).

MATERIALS AND METHODS:

The study groups were determined as control, BPA, MEHP, BPA+MEHP. Cytotoxicity was determined by MTT assay. Expressions of ER stress marker proteins (PERK, Grp78, XBP1 and CHOP) in both cytoplasmic and nuclear cell fractions were determined by Western blotting. The expression profiles were quantitated by using ImageLab program.

RESULTS:

HepG2 cells were exposed to BPA, MEHP and BPA+MEHP at different concentrations for 24 h. Median inhibitory concentrations (IC50) of BPA, MEHP and MEHP+BPA were found to be 615 µg/ml, 17.4 µg/ml and 15+500 µg/ml, respectively. Inhibitory concentration 30 (IC30) for BPA, MEHP and MEHP+BPA were found to be 343 µg/ml, 4.5 µg/ml and 10+400 µg/ml, respectively. In cytosolic fraction, there was only an increase in Grp78 protein expression only in MEHP and BPA-exposed HepG2 cells when IC30 doses were applied. In nuclear fraction, we observed increases in all of ER stress related protein expressions in BPA-exposed cells. However, MEHP caused a slight increase in only Grp78 expression. In BPA-MEHP-exposed cells, PERK, XBP1 and CHOP expressions were higher vs. control cells.

CONCLUSIONS:

Both BPA and MEHP are cytotoxic in HepG2 cells after 24 h. These chemicals can cause induction of ER stress-related proteins, mostly in nuclear cellular fractions. Combined exposure to these compounds seems to aggravate their cellular toxicity. Comprehensive studies are needed to enlighten the toxicity mechanisms of these chemicals and combined exposures should be taken into account when assessing their toxic effects on biological systems.

OP-115: SURFACE-ENHANCED RAMAN SPECTROSCOPY BASED DETECTION STRATEGIES FOR GROUP A STREPTOCOCCUS PYOGENES

[1] Eryilmaz, M., [2] Soykut Acar, E., [3] Cetin, D., [4] Suludere, Z., [5] Boyaci, IH., [1] Tamer, U.

[1]Gazi University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

[2]Abant Izzet Baysal University, Yenicaga Vocational High School, Bolu, Turkey

[3]Gazi University, Faculty of Education, Science Teaching Program, Ankara, Turkey

4Gazi University, Faculty of Science, Department of Biology, Ankara, Turkey

5Hacettepe University, Department of Food Engineering, Ankara, Turkey

INTRODUCTION:

Group A beta-hemolytic Streptococcus pygogenes is the main cause of acute pharyngitis and patients are tested by either a throat culture or a rapid antigen detection (1). However, it takes 48 hours to obtain results and if there are any negative test results, there is a verification needed (2). In this study, a batch analysis was performed to detect the bacteria in the presence of modified nanoparticles using surface-enhanced Raman spectroscopy (SERS) and then, lateral flow immunoassay (LFIA) test strips were prepared for more accurate and a fast detection.

MATERIALS AND METHODS:

Magnetic gold nanoparticles and rod-shaped gold nanoparticles were synthesized for the batch analysis and they were modified with antibody of the target bacteria. LFIA test strips were constructed with different membranes including a sample pad, a conjugation pad, test area and an absorbent pad. Raman reporter labeled gold nanoparticles were employed as a capture probe in the conjugation pad and color change on the test zone was the sign of group A Streptococcus. In addition, the SERS signal of the reporter was evaluated as a confirmation of the target. Different cell concentrations (15-1x108 cfu/mL) were used for quantitative detection of group A Streptococcus by using plotted calibration curve for both systems.

RESULTS:

In batch analysis, interaction time of cotton swab in the bacteria culture was one minute. Modified magnetic gold nanoparticles caught the bacteria in 15 minutes and after 10 minutes of washing, final immunoassay reaction was 30 minutes of time. It was clear that it took 75 minutes to quantify the bacteria with a LOQ of 400 cfu/mL in the batch system. Therefore, the obtained results were the basis for LFIA test. In LFIA strips, it was shown that SERS enabled more sensitive detection of Group A Streptococcus. Comparing the commercial strips, 2x102 cfu/mL of bacteria could be detected and there was no need for verification with the plate counting technique.

CONCLUSIONS:

Both colorimetric and SERS detection of Group A Streptococcus were performed for the first time. The SERS signal enabled the fast and more accurate detection with a lower detection limit comparing the conventional methods.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK-COST CA15114-114Z783.

REFERENCES:

1. Bisno AL (2001). New England Journal of Medicine, 344(3):205-211.
2. Bisno et al., (1997). Clin Infect Dis., 25(3): 574-83.

OP-116: A-GLUCOSIDASE INHIBITORY EFFECTS OF SOME FUNCTIONALIZED AMINO ACID DERIVATIVES

Uysal, S., Ayan, EK., Soyer, Z.

Ege University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Izmir, Turkey

INTRODUCTION:

According to the first World Health Organization (WHO) Global report on diabetes, it caused 1.5 million deaths worldwide in 2012 and type 2 diabetes mellitus (T2DM) is the most common form in the society (1). As it is known, only three agents namely acarbose, voglibose and miglitol are used in the treatment of T2DM by the way of inhibition of α-glucosidase but they have various side effects. Therefore, there is an urgent need to discover and develop new chemical agents with enhanced activity profile and reduced side effects. For this purpose, in this study, as functionalized amino acid derivatives, fourteen 2/3-(acylamino)propionanilide derivatives (Figure 1) have been prepared and evaluated for their α-glucosidase inhibitory activities.

MATERIALS AND METHODS:

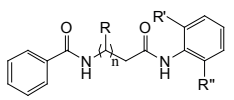
The synthesis of the title compounds was realized in 2 steps. Structures of the compounds were confirmed by spectral (UV, IR, 1H NMR, MS) and elemental analyses. All compounds were evaluated with regard to α-glucosidase inhibition compared to acarbose as reference compound. The enzyme inhibition assay was carried out spectrophotometrically by using slightly modified method of Zawawi et al (3)

RESULTS:

Based on biological activity results, most of the tested compounds showed moderate to weak α-glucosidase inhibitory activity in comparison to the acarbose.

CONCLUSIONS:

A series of 2/3-(acylamino)propionanilide derivatives have been evaluated for their α-glucosidase inhibitory activity profile. The biological activity results demonstrated that further structural modification of this class of functionalized amino acid derivatives may lead to a promising anti-diabetic candidate molecule.



(n=1, R=CH_3)
(1) R'=H R"=H
(2) R'=H R"=Cl
(3) R'=H R"=CH_3
(4) R'=H R"=OCH_3
(5) R'=H R"=CH_2CH_3
(6) R'=H R"=$CH(CH_3)_2$
(7) R'=CH_3 R"=CH_3

(n=2, R=H)
(8) R'=H R"=H
(9) R'=H R"=Cl
(10) R'=H R"=CH_3
(11) R'=H R"=OCH_3
(12) R'=H R"=CH_2CH_3
(13) R'=H R"=$CH(CH_3)_2$
(14) R'=CH_3 R"=CH_3

Figure 1

ACKNOWLEDGEMENTS:

This study was supported by research grant from Ege University (Project Number: 17-ECZ-019)

REFERENCES:

1. Global report on diabetes (2016). ISBN 978 92 4 156525 7 (NLM classification: WK 810). World Health Organization.
2. Kasturi et al., (2017). Bioorganic & Medicinal Chemistry Letters,27: 2818-2823.
3. Zawawi et al., (2017). Bioorganic Chemistry, 70:184-191.

OP-117: IN VITRO APPROACHES TO EVALUATE THE IRRITATION POTENTIAL OF ELECTROLYZED WATER FOR SKIN AND EYE: A BIOCOMPABILITY STUDY

[1,2] Reis, R., [1] Sipahi, H., [1] Kavaz, T., [3] Turkay, O., [3] Ozcelik, H., [1] Aydin, A.

[1] Yeditepe University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, İstanbul, Turkey

[2] Karadeniz Technical University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Trabzon, Turkey

[3] Gebze Technical University,Department of Environmental Engineering, Kocaeli, Turkey.

INTRODUCTION:

Electrolyzed Water (EW) is a novel technology based on electrolysis of water containing sodium chloride or potassium chloride in an electrolysis chamber where anode and cathode electrodes are separated by an ion-permeable diaphragm (1). EW produced in a variety of forms is widely used as a sanitizer, sterilizer for surgical and dental equipment, topical disinfectant and to treat contaminated water (2, 3). The use of the EW is particularly important because chemical disinfectants such as benzalkonium chloride, formaldehyde and glutaraldehyde are potentially toxic to human and corrosive to application area (4). In the present study, we have evaluated antimicrobial activity of three types of EWs and then their biocompability was assessed by cytotoxicity, ocular irritation and skin irritation assays in vitro.

MATERIALS AND METHODS:

The EWs are produced by the electrolysis of tap water containing 5 g/L of sodium chloride in a divided electrochemical reactor. Three types of EWs as acidic (A-EW), slightly acidic (Sa-EW) and mixed (M-EW) were freshly prepared. Microbiological assay was performed according to TS EN 1276 and TS EN 1650 standards on Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa and Candida albicans. Cell viability was tested on mice fibroblast cell line (L929, ATCC) for 24 h exposure to serial dilutions of 10% EWs (v/v) and the viability was determined with MTT assay. To evaluate the potential ocular irritancy of EWs, ICCVAM recommended Hen's Egg Test - Chorioallantoic Membrane (HET-CAM) test method was applied and reactions on the CAM were scored according to lysis, hemorrhage and coagulation within 300 sec of EW exposure. To predict skin irritation potential of EWs, ECVAM validated reconstructed human epidermal model EpiDerm™ (EPI-200, MatTek) was used.

RESULTS:

In microbiological assay, A-EW, Sa-EW, M-EW provided complete bacteria inactivation in 10 minutes. In cytotoxicity assay, no significant difference was observed between EW groups. In HET-CAM assay, none of tested EWs caused ocular irritation according to testing score. Besides, skin irritation test showed that none of tested EWs caused dermal irritation compared to positive control (5% SDS).

CONCLUSIONS:

Based on the biocompability results presented in our study, EWs are not cytotoxic and has no irritating and corrosive properties. Accordingly, EWs can reliably be used as an alternative disinfectant agent.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (1002-116Z169).

REFERENCES:

1. Rasco B (2015). Electrolyzed Water Applications in Aquaculture and the Seafood Industry. J Aquac Res Development, 6:1
2. Yahagi N, Kono M, et al., (2000). Effect of Electrolyzed Water on Wound Healing. Artif. Organs, Vol:2 4(12):984-7.
3. Bui VN, Nguyen KV. et al., (2017). Potential of electrolyzed water for disinfection of foot-and-mouth disease virus. J. Vet. Med. Sci.9(4): 726–729
4. Hao XX, Li BM, et al., (2013). Disinfection effectiveness of slightly acidic electrolysed water in swine barns. Journal of Applied Microbiology. 115, 703-710

OP-118: LFIA ENUMERATION OF E.COLI USING FE3O4/AU-PEI NANOPARTICLES IN BLOOD

[1] Ilhan, H., [2] Dogan, U., [3] Suludere, Z., [4] Boyaci, IH, [5] Cetin, D., [1] Saglam, N., [2] Tamer, U.

[1]Hacettepe University, Department of Nanotechnology and Nanomedicine, Ankara, Turkey

[2]Gazi University, Department of Pharmacy, Ankara, Turkey

[3]Gazi University, Department of Biology, Ankara, Turkey

4Hacettepe University,Department of Food Engineering, Ankara, Turkey

5Gazi University Science Teaching Programme, Faculty of Education, Ankara, Turkey

INTRODUCTION:

Paper based microfluidic systems are one of the most commonly utilized commercial test kits for the determination of bacteria, drugs of abuse and pregnancy etc. because of its low cost, simplicity and user-friendliness advantages. Most of these lateral flow immunoassay systems has been used for qualitative detection, but various new paper based biosensor systems have been developed by using fluorescence, electrochemistry and SERS etc. for the quantitative investigations (1). Magnetic nanoparticles have been used as a powerful way in various bioassays and used as solid support owing to its advantages such as biocompatibility, stability and immunomagnetic extraction. Modification of these nanoparticles enable to straightforward conjugation with bacteria or biomolecules of interest (2).

MATERIALS AND METHODS:

Casein modified Fe3O4/Au-PEI nanoparticle provides immunomagnetic separation and specific detection of the target bacteria. Enzyme substrate is covalently linked between magnetic particle and target bacteria to cleave bond easily using an enzyme. Then, magnetic nanoparticle is cleaved from E. coli in order not to prevent bacteria movement on the test strip. The magnetic particles are removed by a magnet, and E.coli can be detected efficiently on the test strips. E.coli is also labeled with DTNB to enable SERS signals on the test strip. Test line is spotted with E. coli antibody in order to catch labelled bacteria (3).

RESULTS:

The SERS signals were obtained and calibration curve was plotted by using SERS peaks area at 1330 cm-1 versus logarithmic initial bacteria concentrations. This method was applied to E.coli spiked blood with different concentrations. The selectivity of this developed biosensor system was investigated by applying the same procedure to Salmonella enteritidis and Bacillus subtilis solutions. The results obtained for the SERS intensities of different bacteria were measured to be compared with the SERS signals acquired for E.coli as demonstrated in Fig 1.

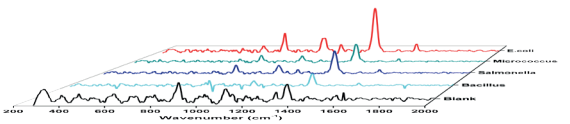


Figure 1. SERS signals of Selectivity of Different Bacteria

CONCLUSIONS:

This new nano-immunomagnetic extraction for paper based system can be used in many application areas including food quality, water contamination, clinical diagnosis and environmental monitoring due to its attractive advantages such as simple, low-cost, portable and disposable features.

ACKNOWLEDGEMENTS:

TUBITAK Cost-CA15114 – 114Z783

REFERENCES:

1. Guven B, Akgul N, Temur E, Tamer U, BoyaciIH (2011). Analyst, 136:740-748
2. Temur E, Boyaci IH, Tamer U, Unsal H, Aydogan N (2010). Anal Bioanal Chem, 397: 1595-1604
3. Ren W, Cho IH, Zhou Z, Irudayaraj J (2016). Chemcom, 52: 4930.

OP-119: NEW THIAZOLE DERIVATIVES AS POTENTIAL ALDOSE REDUCTASE INHIBITORS.

[1] Sever, B., [1] Altintop, MD., [2] Beydemir, S., [3] Demir, Y., [1] Ozdemir, A.

[1] Anadolu University, Department of Pharmaceutical Chemistry, Eskisehir, Turkey

[2] Anadolu University, Department of Biochemistry, Eskisehir, Turkey

[3] Ataturk University, Department of Chemistry, Erzurum, Turkey

INTRODUCTION:

Aldose reductase (ALR2), the first and rate limiting enzyme of the polyol pathway, is responsible for NADPH-dependent reduction of glucose to sorbitol. Blocking the polyol pathway of glucose metabolism related to inhibition of ALR2 has been reported to be effective in reducing long-term diabetic complications including retinopathy, nephropathy, neuropathy and cataract (1). Due to the significance of thiazole scaffold for antidiabetic drug design (2), we aimed to design and synthesize new thiazole-based ALR2 inhibitors.

MATERIALS AND METHODS:

New thiazole-based compounds 1-12 were synthesized via the ring closure reaction of 3,4-dihydro-2H-1,5-benzodioxepine-7-carbaldehyde thiosemicarbazone with aryl acyl bromides. These compounds were evaluated for their in vitro inhibition behaviors on ALR2 which was purified from rat liver using several chromatographic methods. Then, Ki parameters were determined via Lineweaver–Burk (1/*V*–1/[S]) graph (3). Moreover, molecular docking studies were performed for the most effective compound in the active site of ALR2 (PDB code: 3O3R) and in silico ADME studies were also carried out (4).

RESULTS:

4-(4-Cyanophenyl)-2-[2-((3,4-dihidro-2*H*-1,5-benzodioxepin-7-yl)methylene)hydrazinyl]thiazole (**3**) was detected as the most potential ALR2 inhibitor in this series with the K_i constant value of 0,018±0,005 μM and the compound showed competitive inhibitory activity. Molecular docking studies indicated that compound **3** presented hydrogen bonds with Asp217, Gln184 and Lys22 residues in the active site of ALR2. Besides, ADME results revealed that all compounds were within the acceptable range intended for human use.

CONCLUSIONS:

Both in vitro and in silico studies emphasize that compound 3 stands out as a potential orally bioavailable ALR2 inhibitor for further studies.

REFERENCES:

1. Hussain et al., (2014). Bioorganic Med. Chem. Lett., 24:2086-2089.
2. Ayati et al., (2015). Eur. J. Med. Chem., 97: 699-718.
3. Demir et al., (2017). J. Biochem. Mol. Toxicol., 31: doi: 10.1002/jbt.21935.
4. Schrödinger Release 2016-2: Schrödinger, LLC, New York, NY, USA.

OP-120: LIVE ORGANIC SPICE-DERIVED FLAVORINGS IN NUTRITIONAL PHARMACOLOGY

[1] Gavrylova, I., [2] Onder, A., [1] Protsenko, O., [1] Zazhyhina, K.

[1]Functional Food Researcher and Evangelist in the Field of Natural, & Eco-tech Sciences, Kiev, Ukraine

[2]Ankara University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

Live organic spice-derived flavorings are a category of palatability defining ingredients vital in nutritional pharmacology. They are used in the production of functional foods for preventive and therapeutic treatments (1-3). The aim of the study is to prove that palatability and variety of foods are important and health-wise can be achieved by application of ingredients that are safe, sustainable and have recognizable properties. Therefore, flavorings derived from some spices are analyzed in the context of actual examples in health food and fitness industry. Briefly, the eco-tech oil extraction has been mentioned together with the other necessary details and experiences.

MATERIALS AND METHODS:

The study has been carried out firstly via market survey with spice material collection. Then, the spices have been validated by expert examinations. The oil spices have been subjected to innovational eco-tech oil extraction. In the laboratory studies, the spices and oils have been tested, then performed data analysis and economic analysis – data and reports displayed in the study.

RESULTS:

Live spice-derived flavorings serve as important ingredients for functional foods due to their bioactive content as well as stimulation of pleasure gained from food via improvements in palatability. “Let food be your medicine” is the moto of superfoods these days while nutritional pharmacology has always been a vivid but silent part of the food industry and now it becomes officially powerful with the help of spices and spice-derived components getting popular in the modern world.

CONCLUSIONS:

Live spice-derived flavorings are the next stage of evolution of functional aromas and flavors and are a perfect solution for nutritional pharmacology and ingredient dilemmas with diverse positive effects on human health and wellbeing as well as marketing attraction and business solution for a wide range of nutrition-focused businesses.

ACKNOWLEDGMENTS

This study has been supported by Bulgarian Ministry of Food and Agriculture and the community of berry professionals in Ukraine.

REFERENCES

1. Katan M, De Roos N (2004). Critical Reviews in Food Science and Nutrition. 44:369–377.
2. Kalpana P, Srinivasan K (2004). J Med Res. 119: 167-179.
3. Brown A (2011). In: Cengage Learning Inc. Understanding Food. Principles and preparation. 4th Edition, Chapters: Food Evaluation. 23-30, Chemistry of Food Composition. pp. 31-63.

OP-121: INVESTIGATION OF MITOCHONDRIAL RESPIRATION DYSFUNCTION CAUSED BY SOME DRUGS

Arzuk, E., Orhan, H.

Ege University, Department of Pharmaceutical Toxicology, Izmir, Turkey

INTRODUCTION:

Mitochondria are cell energy powerhouses and produce ATP by oxidative phosphorylation (OXPHOS). Mitochondria may be the targets of multiple drugs and chemical substances due to their unique structure and substantial functions (1).The aim of our study was to assess the mitochondrial toxicity of eight drugs (clozapine -CLZ-, olanzapine -OLA-, nifedipine -NIF-, diclofenac -DIC, valproic acid -VPA- dapson -DAP, tiaprofenic acid -TIA-, and sulfafenazol -SULP) by oxygen consumption rate (OCR) measurement.

MATERIALS AND METHODS:

In our experiments, CHO-K1 cells were used as an in vitro model. The cells were treated with three final doses (1, 10, and 100 µM) of test drugs during 16 hours. OCR measurement was performed by Luxcel Biosciences' MitoXpress® Xtra Oxygen Consumption Assay (2).

RESULTS:

DAP, TIA and VPA at 100 µM, and OLA at 10 and 100 µM caused significant decrease in OCR compared to control.

CONCLUSIONS:

Our results suggest that DAP, TIA, VPA and OLA interfere with mitochondrial respiration and therefore may lead to mitochondrial dysfunction. The determination of mechanism(s) of drugs' toxicity is also useful for preventing potential adverse effects. Thus, further studies are underway in our laboratory to investigate whether additional mechanisms play a role in in vitro, and possibly in vivo toxicity of these drugs

ACKNOWLEDGEMENTS:

This study was supported by TUBITAK, grants 114S310.

REFERENCES:

1. Olszewska A, Szewczyk A (2013). Mitochondria as pharmacological target: magnum overview. IUBMB Life, 65: 273-81.
2. Komulainen T, Lodge T, et al., (2015). Sodium valproate induces mitochondrial respiration dysfunction in HepG2 in vitro cell model. Toxicology, 331:47-56.

OP-122: NEW PURINE AND PYRIMIDINE NUCLEOSIDE ANALOGS: SYNTHESIS AND CYTOTOXIC ACTIVITY ON SELECTED HUMAN CANCER CELL LINES

[1] Altiparmak, D.,[1] Tuncbilek, M.,[2] Durmaz,I., [3] Cetin-Atalay, R.

[1] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

[2] Bilkent University, Department of Molecular Biology and Genetics, Ankara, Turkey

[3] Middle East Technical University, Bioinformatics Department, Ankara, Turkey

INTRODUCTION:

Cytotoxic nucleoside analogues and nucleobases are a pharmacologically diverse family, which has grown to include a variety of purine and pyrimidine nucleosides with activity in both solid tumours and malignant disorders of the blood (1, 2). These agents have many intracellular targets to induce cytotoxicity: they behave as antimetabolites, competing with physiological nucleosides during DNA or RNA synthesis, and as inhibitors of key cell enzymes (2, 3).

MATERIALS AND METHODS:

In this study, we synthesized novel purine and pyrimidine ribonucleoside analogs as putative cytotoxic agents. The 5', 6-disubstituted 9-(β-D-ribofuranosyl)purine derivatives were readily obtained from commercially available inosine in seven steps and the 4-substituted-1-(β-D-ribofuranosyl)-2(1H)-pyrimidinone derivatives were prepared from uracil/thymine in four steps in very cost effective synthesis approach. The newly obtained compounds were characterized for their cytotoxicity in human cancer cell lines. The cytotoxicities of the compounds were initially analyzed on liver (Huh7), colon (HCT116) and breast (MCF7) carcinoma cell lines by SRB assay for determining the IC50 values. The IC50 values after 72 hours of treatment with each molecule were also calculated in comparison with DNA topoisomerase inhibitor camptothecin (CPT), the nucleobase analog 5-fluorouracil (5-FU) and nucleoside analogs fludarabine, cladribine, pentostatine.

RESULTS:

N6-Bromophenylsulfonyl purine nucleoside analog demonstrated significant cytotoxic activity for the cell lines tested and was more cytotoxic (IC50 = 1.5-30.8) than 5-FU, fludarabine on Huh7, HCT116 and MCF7 cell lines. We then tested the cytotoxic effect of the most potent nucleoside derivative on additional hepatocellular carcinoma (HCC) cell lines: Huh7, Hep3B, HepG2, PLC, Mahlavu, FOCUS, SNU475, SNU182, SNU387, SNU398, SNU423 and SNU449. N6-(4-Bromophenyl)sulfonylpiperazine derivative displayed the best cytotoxic activity, with IC50 values

of 15.5-22.5 μM against Hep3B and SNU423 cell lines and had a better cytotoxic activity than Fludarabine and Pentostatine on Hep3B and SNU423 cell lines.

CONCLUSIONS:

A series of new purine and pyrimidine nucleoside analogs were prepared and their cytotoxic activities identified. 6-(4-bromophenyl)purine derivative showed potent anticancer activity at low concentrations against Huh7, HCT116, MCF7 cell lines when compared to 5-FU and Fludarabine as potent cytotoxic drugs. Among the 47 compounds investigated, the most potent purine and pyrimidine derivatives were further analyzed for their activity on HCC cells. The molecule bromo analog exhibited promising cytotoxic activity with IC50 value of 15.5 μM on Hep3B cell line.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-112S182)

REFERENCES:

1. Galmarini CM, Mackey JR, Dumontet C (2002). The Lancet Oncology, 3:415-424.
2. Demir Z, Bilget Guven E, Ozbey S, Kazak C, Cetin Atalay R, Tuncbilek, M (2015). European Journal of Medicinal Chemistry, 89:701-720.
3. Robak P, Robak T (2013). Cancer Treatment Reviews, 851-861.

OP-123: INVOLVEMENT OF REACTIVE METABOLITES IN CYTOTOXIC EFFECTS OF VARIOUS FREQUENTLY USED DRUGS IN VITRO

Erguc, A., Mutlu, N., Arzuk, E., Karakus, F., Orhan, H.

Ege University, Department of Pharmaceutical Toxicology, Izmir, Turkey

INTRODUCTION:

Cytotoxicity tests provide information about test compounds to us whether they have toxic effects when incubated under the defined conditions in the cell culture (1). In the present study cytotoxicity of eight drugs (clozapine, olanzapine, nifedipine, diclofenac, valproic acid, dapson, tiaprofenic acid and sulfaphenazole) were investigated by using the MTT and LDH leakage assays at three dose levels (1, 10, 100 μM). MTT test was also carried out in the presence and absence of GSH (soft nucleophile) and KCN (hard nucleophile) in order to figure out whether cytotoxicity of these drugs are caused by reactive metabolites (RM) of the test drugs.

MATERIALS AND METHODS:

In both assay CHO-K1 cells were used as an in vitro model. The cells were treated with test drugs (1, 10. 100 μM) with/without trapping agent and incubated for 16 hours. After incubation cells were treated with MTT for 4 hours. Then DMSO was added to dissolve the formazan crystals. The optic dansity was read at 570 nm (2). In LDH leakage assay, NADH (300 μM) and Na-pyruvate (770 μM) were added to medium taken from the wells after 16 hours incubation. The changes of NADH absorbance was monitored at 340 nm for 4 minutes (3).

RESULTS:

In MTT, Clozapine and Nifedipine at 100 μM and Diclofenac at three doses led to significant decrease when compared to control. In addition, presence of both trapping agents prevented cytotoxicity, which suggested the occurrence of RMs in this effect. In LDH, Clozapine and Nifedipine at 100 uM caused considerable toxicity similarly in MTT.

CONCLUSIONS:

Clozapine and Nifedipine showed substantial toxicity at 100 μM. They need to be investigate of toxicity mechanism to overcome the adverse effects.

ACKNOWLEDGEMENTS:

This study was supported by TUBITAK, grants 114S310.

REFERENCES:

1. Riss TL, Moravec RA, et al., (2011). Cytotoxicity Testing: Measuring Viable Cells, Dead Cells, and Dedecting Mechanism of Cell Death. Methods In Molecular Biology. 740:103-14
2. Mosmann T (1983). Rapid Colorimetric Assay for Cellular Growth and Survival: Application to Proliferation and Cytotoxicity Assays. Journal of Immunological Methods. 65:55-63
3. Hassoun EA, Roche VF, et al., (1993). Release of Enzymes by Ricin From Macrophages and Chinese Hamster Ovary Cells in Culture. Toxicology Methods. 3(2):119-29

OP-124: APPLICATION OF COMPUTER-BASED METHODS TO SEARCH FOR NOVEL SIRTUIN INHIBITORS: POTENTIAL OF NATURAL PRODUCTS

[1,2] Karaman Mayack, B., [2] Alhalabi, Z., [3] Swyter, S.,[4] Mihigo, SO., [5] Andrae-Marobela, K., [3] Jung, M., [2] Sippl, W., [2,6] Ntie-Kang, N.

[1] Biruni University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Istanbul, Turkey

[2] Martin-Luther University of Halle-Wittenberg, Department of Pharmaceutical Chemistry, Halle (Saale), Germany

[3] Albert-Ludwigs-University of Freiburg, Institute of Pharmaceutical Sciences, Freiburg, Germany

[4] University of Kinshasa, Department of Chemistry, Congo

[5] University of Botswana, Department of Biological Sciences, Faculty of Science, Botswana

[6] University of Buea, Department of Chemistry, Cameroon

INTRODUCTION:

Sirtuins are nicotinamide adenine dinucleotide (NAD+)-dependent class III histone deacetylases, which play a role in the pathogenesis of several diseases such as metabolic disorders, neurodegeneration and cancer (1). Structure-based virtual screening (VS) studies on pan-African natural products library (p-ANAPL) (3) led the identification of bichalcones as novel inhibitors of sirtuins. Moreover, we proposed workflows for ligand-based VS campaigns to guide the hit identification and lead optimization of these compounds.

MATERIALS AND METHODS:

Protein structures were prepared by using Protein Preparation Wizard module in Schrödinger. Docking studies were performed using the GOLD and GLIDE programs. Calculation of fingerprints and generation of pharmacophore groups using docked bischalcones were suggessted for further ligand-based VS campaigns.

RESULTS:

Virtual screening of the p-ANAPL database resulted in the identification of two bichalcones, which showed inhibitory activity against both Sirt1 (1; IC50 = 46.7 ± 6.0, 2; IC50 = 40.8 ± 8.5) and Sirt2 (1; IC50 = 48.5 ± 39.5, 2; IC50 = 44.8 ± 5.1). These compounds were selected for futher hit identification and lead optimization via ligand-based VS approaches.

CONCLUSIONS:

Natural products (NPs) or NP derivatives coming from Northern Africa showed a great potential for the identification of novel scaffolds for sirtuins which prompted us to design comprehensive virtual screening campaigns to evaluate the potential of different publicly available naturally occuring compound collections.

ACKNOWLEDGEMENTS:

Z.A. is currently a doctoral candidate financed by the German Academic Exchange Services(DAAD), Germany. F.N.-K. acknowledges a Georg Forster fellowship from the Alexander von Humboldt Foundation, Germany. The Jung and Sippl group thank the German Research Foundation (DFG, within RTG1976, Ju295/14-1 and Si868/15-1) for support. The authors acknowledge the technical support of Conrad V. Simoben.

REFERENCES:

1. Hu, J.; Jing, H.; Lin, H. Sirtuin inhibitors as anticancer agents. Future Med. Chem. 2014, 6, 945–966.
2. Ntie-Kang, F. et al. Virtualizing the p-ANAPL library: A step towards drug discovery from African medicinal plants. PLoS ONE 2014, 9, e90655.

OP-125:TURKISH SEA SPONGES AND THEIR IMPORTANCE

[1] Gözcelioğlu B., [2] Konuklugil B.

[1] Scientific and Technological Research Council of Turkey (TÜBİTAK), Ankara,Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

Drug discovery from marine natural products has gained importance in the past few years. Ziconotide, a peptide originally discovered in a tropical cone snail, was the firstmarine-derived compound to be approved in the United States, in December 2004, for pain treatment. In October 2007, trabectedin became the first marine anticancer drug. Approximately 10–15 different marine natural products are currently in clinical trials, mostly in the areas of cancer, pain or inflammatory diseases (1,2). Among the groups of marine invertebrates, the sponges (Phylum Porifera) are receiving much attention mainly because of the unique natural compounds characterized by a huge variety of biological activities such as; antioxidant, antiviral, antibacterial, antifungal, antitumor, anticancer, antifouling activities which acts as potential natural compounds of interest for pharmaceutical applications (3-5).Turkish coastline is almost 8400 km long in total. The sponges found in the seas surrounding Turkey have not yet been intensively studied. During the course of our studies on Turkish marine sponges, we have identified 4 new species and isolated some secondary metabolites from marine sponges extracts collected from the different costs of Turkey.

MATERIAL AND METHODS:

12 sponges were collected from different locations, at depths varying from 10-30 m by scuba diving. The sponges were collected and identified by Dr. Bulent

Gozcelioglu. Sponge samples were deposited at Ankara University, Faculty of Pharmacy, Ankara, Turkey.

RESULTS:

We have identified 4 new species and isolated some secondary metabolites from marine sponges extracts collected from the different costs of Turkey

CONCLUSIONS:

Studies on Demospongiae diversity in the Aegean and Mediterranean coast of Turkey are scarce. During our search for Turkish marine sponges, we have identified new species and also isolated several secondary metabolites from five different marine sponges which have been collected from the different costs of Turkey

REFERENCES:

1. Mayer AM, Glaser KB, Cuevas C, Jacobs RS, Kem W (2010). Trends in Pharmacological Sciences, 31:255-265.
2. Perdicaris S, Thomais V, Athanasios V (2013). Natural Products Chemistry and Research,1:(3)1-8.
3. Blunt JW, Copp BR, Hu WP, Munro MH, Northcote PT, Prinsep MR (2007). Natural Product Reports,1:31-86:31-86.
4. Mayer, A, Rodríguez A D, Taglialatela-Scafati, O, Fusetani N (2013). Marine Drugs, 11:2510-2573.
5. Martins A, Vieira H, Gaspar H, Santos S (2014). Marine Drugs, 12:1066-01.

OP-126: SEMI-RAPID MAXILLARY EXPANSION ORTHODONTIC TREATMENT DECREASED KALLIKREIN-1 LEVELS IN CHILDREN WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

[1] Kaya-Sezginer E., [1] Bakar-Ates F., [2] Hoxha S., [2] Toygar-Memikoğlu U.

[1]Ankara University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey

[2]Ankara University, Faculty of Dentistry, Department of Orthodontics, Ankara, Turkey

INTRODUCTION:

Obstructive sleep apnea syndrome (OSAS) is a prevalent disease in children, defined by habitual snoring associated with prolonged, repeated events of partial and/or complete upper airway obstruction, hypercapnia and hypoxemia during sleep (1). Rapid maxillary expansion (RME) is an efficient orthodontic treatment approach for the treatment of OSAS in children with maxillary constriction (2, 3). The purpose of this study was to investigate the effect of semi-rapid maxillary expansion (SRME) orthodontic treatment on levels of some biomarkers related with OSAS.

MATERIALS AND METHODS:

Thirty children with OSAS were included in this study. Fifteen children were enrolled as control, and 15 children were subjected to SRME orthodontic treatment method for 5 months. The levels of OSAS biomarkers in serum and urine were measured.

RESULTS:

Serum kallikrein (KLK)1 levels decreased significantly in the treatment group. There was a significant increase in serum orosomucoid (ORM)2 levels and a decrease in urine perlecan levels in the control group after a 5-month follow-up. A significant negative correlation between serum ORM2, perlecan, gelsolin, and KLK1 levels and intercanin width, as well as between serum ORM2 and KLK1 levels and intermolar width, was observed.

CONCLUSIONS:

The results of this study indicated that KLK1 and ORM2 levels are important biomarkers to evaluate in children with OSAS. A further investigation of OSAS-related biomarkers and their relationship with orthodontic parameters is needed for providing easier and reliable modulatory strategies in the treatment of OSAS.

ACKNOWLEDGEMENTS:

This study was supported by Ankara University Scientific Research Foundation with 13L3334002 project number.

REFERENCES:

1. ozal et al., (2009). American Journal of Respiratory Critical Care Medicine, 180(12):1253-61.
2. Pirelli et al., (2004). Sleep, 27(4):761-6.
3. Villa et al., (2011). Sleep Breathing, 15(2):179-84.

OP-127: INVESTIGATION OF CYTOTOXIC/ APOPTOTIC EFFECTS OF AZD3463, A NEW ALK/IGF-1R DUAL INHIBITOR, IN BREAST CANCER CELL LINE

[1] Demir, B., [2] Ozates, NP., [2] Biray Avcı, C., [2] Gunduz, C., [1] Karadagli Sozer, S., [1] Erciyas Lermioglu, F.

[1]Ege University, Department of Pharmaceutical Toxicology, Izmir, Turkey

[2]Ege University, Department of Medical Biology, Izmir, Turkey

INTRODUCTION:

Targeting multiple signaling pathways for development of new drugs seems the best strategy for managing cancer. AZD3463 is a potent ALK/IGF-1R inhibitör and shows oncogenic activity via activation of PI3-kinase/AKT pathway or by inhibition of apoptosis (1). We aimed to investigate the cytotoxic/apoptotic activity of AZD3463 in MCF-7 cell line and underlying mechanism regarding the implication of ALK and IGF-1/IGF-1R pathways in the development of breast cancer (2,3).

MATERIALS AND METHODS:

In our experiments, MCF-7 is used as an in vitro model of human breast cancer cells. MCF-7 cells were treated with dose range of 0,39μM to 50μM AZD3463 during 24, 48, 72 hours and cytotoxicity was evaluated by using WST-1 assay. Using IC50 dose, apoptotic effects of AZD3463 were assessed by flow cytometric analysis. We investigated the alterations of gene expressions with qRT-PCR.

RESULTS:

The IC50 dose of AZD3463 was determined as 0.765μM for 72nd hour. Results showed that IC50 dose of AZD3463 induced apoptosis 2.4 fold when compared to control cells that untreated with AZD3463. In addition, qRT-PCR results showed that the expression of PTEN, an important tumor suppressor gene, increased 9,75 fold and ILK, IRS1, PIK3R2, MTCP1, HRAS, MAPK3 genes which associated with PI3K/AKT pathway and cancer progression decreased 2.03, 2.02, 3.7, 2.7, 2.02, 2.43 fold, respectively in MCF-7 cells treated with AZD3463 to control cells.

CONCLUSIONS:

These novel findings show that AZD3463 has an important role in preventing breast cancer progression and could be used as a pioneering target agent in breast cancer treatment.

ACKNOWLEDGEMENTS:

This study was supported by Ege University Coordinatorship of Scientific Research Projects (17-ECZ-018).

REFERENCES:

1. Powers C, Aigner A, et al., (2002). Pleiotrophin signaling through anaplastic lymphoma kinase is rate-limiting for glioblastoma growth. J Biol Chem. 277:14153–8.
2. Robertson FM, Petricoin EF, et al., (2013). Presence of anaplastic lymphoma kinase in inflammatory breast cancer. Springerplus. 2:497.
3. Ochnik AM, Baxter RC (2017).Insulin-like growth factor receptor and sphingosine kinase are prognostic and therapeutic targets in breast cancer. BMC Cancer. 17: 820.

OP-128: EXPLORING CELL DEATH MECHANISM IN A375 HUMAN MALIGN MELANOMA CELLS UPON TREATMENT A MANNICH BASE DERIVATIVE

[1] Ercan, A., [2] Aytemir MD.

[1] Hacettepe University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey

[2] Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Che mistry, Ankara, Turkey

INTRODUCTION:

Having high mortality rates and increasing prevalence malign melanoma is one of the most aggressive types of cancer and is responsible for 75 % of skin cancer-related deaths. Characterized by melanin accumulation, one approach to prevent this process is tyrosinase inhibition. Kojic acid, a potent inhibitor of tyrosinase, currently features in dermocosmetics used against hyperpigmentation. In our previously study, chlorination of the 2-hydroxymethyl moiety of kojic acid using thionyl chloride at room temperature produced chlorokojic acid (2-chloromethyl-5-hydroxy-4H-pyran-4-one), with the ring hydroxyl being unaffected. Mannich base with the structure of 6-chloromethyl-2-((3,4-dichlorobenzyl)piperazin-1-yl) methyl-3-hydroxy-4H-pyran-4-one (compound 1) was synthesized by the reaction of chlorokojic acid and substituted 3,4-dichlorobenzylpiperazine in presence of formaline at room temperature. Compound 1 has high antibacterial and antiviral activity (2). Especially, compound 1 appeared the most active derivative against Parainfluenza-3 virus.

In addition, cytotoxic effects of Compound 1 on A375 human malignant melanoma, HGF-1 human gingival fibroblasts and MRC-5 human lung cell lines were investigated. The results of cytotoxicity have been patented (3). In the presented work we aimed to clarify the cell death mechanism at the cellular and genomic level.

MATERIALS AND METHODS:

Cultured A375 cells were treated with compound 1 or vemurafenib, a commercially avalable drug used in malign melanoma treatment. SRB assay was conducted in order to detect cytotoxicity. Cells treated with reagents were subjected to flow cytometry analysis. RT-PCR was performed in order to determine the gene expression levels of specific genes of the apoptotic pathway.

RESULTS:

Apoptotic, necrotic and live cell populations were detected following flow cytometry measurement. The gene expression levels of apoptotic proteins were normalized against housekeeping gene GAPDH.

CONCLUSIONS:

Compared to Vemurafenib which is a gold standard, Compound 1 previously synthesized by our team is a promising agent against human malign melanoma, as it triggers controlled cell death mechanisms without harming healthy cell lines.

ACKNOWLEDGEMENTS:

This study was supported by Hacettepe Research Fund (THD-2018-17033)

REFERENCES:

1. Chang TW, Weaver AL, Brewer JD, Kyle RA, Baum CL (2017). J. Am. Acad. Dermatol.,
2. Aytemir MD, Ozcelik B (2010). European Journal of Medicinal Chemistry, 45(9):4089-95.
3. Aytemir M, Karakaya G, Ercan A, Oncul S, Anticancer and Antityrosinase Activities of Kojic Acid Derivatives-Turkish Patent TR2017/20155.

OP-129: IN VITRO BIOCOMPATIBILITY OF FLOWABLE BULK-FILL DENTAL COMPOSITES

[1] Demirel, G., [1] Gurkan, G.,[2] Demirsoy, F., [2] Altuntas, EG., [2] Yener Ilce, B., [3] Kilicarslan, MA.

[1] Ankara University, Faculty of Dentistry Department of Restorative Dentistry, Ankara, Turkey.

[2] Ankara University Biotechnology Institution, Ankara, Turkey.

[3] Ankara University, Faculty of Dentistry Department of Prosthetic Dentistry, Ankara, Turkey.

INTRODUCTION:

Conventional dental composites are usually placed in 2mm increments to reduce ensure proper light curing. Nevertheless; the incremental technique extends the restoration procedure and increases the risk of air bubble formation between layers. These limitations led to the development of a new class of composite resin type known as “bulk-fill” (1). These materials can be properly photo-polymerized even when applied in thick layers up to 4–5mm. During the light polymerization, not all of the monomers participate in the polymer network. Cytotoxicity mechanisms are predominantly associated with the short-term release of free monomers formed during monomer-polymer conversion(2). The aim of this study was to evaluate the cytotoxicity of bulk-fill composites, with real-time cell vitality.

MATERIALS AND METHODS:

To assess the cytotoxicity of composite materials, L-929 mouse fibroblast cell line was seeded into the wells of E-plate with a concentration of 25000cells/300µl/well. Cell proliferation was performed with Real-Time Cell Analysis and proliferation was monitored for 48 hours.

RESULTS:

Varying degrees of morphologic alterations were observed with the various composites, depending on chemical composition. Among the bulk-fill composites, VBF caused the majority of cells to become small, retracted, and rounded, with condensed and fragmented nuclei morphology, other tested composites had little effects on the cell morphology approximately 70% of cells remained spindle shaped. Varying levels of cytotoxic effects were observed tested composites. At the end of the 48 hours, SDR was significantly more cytotoxic than the other tested composites (Figure 1).

CONCLUSIONS:

In the present study, it was demonstrated that there was a difference among the tested materials when evaluating their cytotoxicity results.

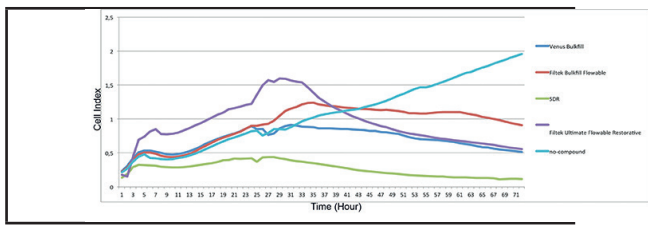


Figure 1: Real-time monitoring of cultured L-929 cells adhesion and cell proliferation.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Ankara University Coordinator of Scientific Research Projects (15B0234001)

REFERENCES:

1. Van Ende A, et al., (2017).Journal of Adhesive Dentistry;19:95-109.
2. Goldberg M (2008). Clinical Oral Investigation;12: 1-8.

OP-130:THE ANTICANCER EFFECTS OF CAMALEXIN-IMATINIB COMBINATION ON MCF-7 BREAST CANCER CELLS

Ozmen, N., Bakar Ates, F.

Ankara University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey.

INTRODUCTION:

Phytoalexins are firstly identified as antimicrobial compounds which are produced as secondary metabolites by plants against various forms of stress (1). Studies have also shown that some phytoalexins may have anticancer effects. Among these, camalexin (CMX) is a natural phytoalexin and it's been demonstrated to mediate cytotoxicity towards aggressive prostate cancer cells (2). Smith et.al. (3) have shown that camalexin induced apoptosis of prostate cancer cells through an alteration on expression and activity of lysosomal protease Cathepsin B. The aim of present study is to evaluate the effects of camalexin in combination with imatinib (IM) on MCF-7 breast cancer cell growth.

MATERIALS AND METHODS:

In order to evaluate the effects of camalexin alone and in combination with imatinib on cell growth, MTT assay was performed. The cells were treated with camalexin alone in a concentration range between 5-50 μM and in combination studies cells were treated with 10 μM camalexin and 3.01 μM imatinib. The effects of combination therapy on cell cycle arrest were measured by cell analyzer. Apoptosis was detected by annexin v binding assay and also by fluorescence imaging studies.

RESULTS:

MTT results showed that camalexin significantly inhibited the growth of MCF-7 cells at 10 μM and higher concentrations ($p<0.01$). The viable cell amount was detected as 77.74±1.61, and 45.89±2.05 for treatments of 10uM CMX, and CMX-IM combination, respectively. The results of cell cycle assay has shown that camalexin induced a cell cycle arrest of MCF-7 cells at S phase.

We also observed that the total apoptotic cell population was significantly increased in combination group, when compared to camalexin and imatinib alone ($p<0.05$).

CONCLUSIONS:

This study has demonstrated that camalexin attenuates the anticancer effect of imatinib against MCF-7 breast cancer cells. Further studies are required to identify the underlying mechanisms of effects.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-216S129).

REFERENCES:

1. Bailey JA, Mansfield JW, editors. (1982). Glasgow UK: Blackie
2. Smith BA, et.al. (2013). Journal of Natural Medicine, 67(3): 607-618.
3. Smith BA, et al. (2015). Molecules, 19(4): 3988-4005.

OP-131: IN-VITRO TOXICITY EVALUATION OF NEONICOTINOID INSECTICIDE ACETAMIPRID ON AR42J PANCREATIC CELL LINE.

Kara, M., Oztas, E., Ozhan, G.

Istanbul University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Istanbul-Turkey

INTRODUCTION:

Neonicotinoid insecticides, nicotinic acetylcholine receptor agonists, have selective toxicity on insects through α4p2 nicotinic acetylcholine receptors (nAChR). They are used 30% part of insecticide marketing in the world. Acetamiprid is one of the selective neonicotinoid insecticides, and is used alone or combination with other pesticides. Its toxic effects and mechanism of action have not been clarified on pancreas, although it is known to have toxic on several organ systems, including the nervous, respiratory and immune systems. It has been reported that LD50 value is the range of 140-417 mg/kg b.w. in rodents, and NOAEL level is 400 ppm in 13 week mice for acetamiprid. There are a few studies about its genotoxic effects (1,2)

MATERIALS AND METHODS:

Cytotoxic and genotoxic effects of acetamiprid on AR42J pancreas cell line in the present study. For cytotoxicity and genotoxicity assays, MTT test and comet assay were respectively performed. 1mM, 2mM, 4mM and 6mM doses were administrated to AR42J cell line. For oxidative stress analysis ROS detection performed by flowcytometry and levels of GSH were determined in the cell homogenates according to the method of Beutler.

RESULTS:

LC50 value was 12,61 mM. According to the results of comet assay performed in the range of 1-70 mM exposure concentration, acetamiprid induced DNA damage in groups depending on concentration. The mean tail intensity values of groups were 1.83 for control 9.83, 16.72, 29.31 and 34.07 for exposure groups. GSH was significantly increased in 6mM dose group.

CONCLUSIONS:

It is believed that the data obtained contributes to the literature due to the lack of research on the potency of acetamiprid's toxic effects on pancreas.

REFERENCES:

1. Matsuda K, Buckingham SD, et al., (2001). Neonicotinoids: insecticides acting on insect nicotinic acetylcholine receptors. Trends Pharmacol Sci. 2001 Nov;22(11):573-80
2. http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Report11/Acetamiprid.pdf
3. Cimino AM, Boyles AL, et al., (2017). Effects of Neonicotinoid Pesticide Exposure on Human Health: A Systematic Review. Environ Health Perspect. 2017 Feb;125(2):155-162.

OP-132: INVESTIGATION OF THE EFFECT OF PUNICALAGIN ON ADIPOCYTE DIFFERENTION

[1] Berkoz, M., [2] Yalin, S., [2] Yildirim, M., [3] Comelekoglu, U., [2] Yalin, AE.

[1] Van Yuzuncu Yil University, Faculty of Pharmacy, Department of Biochemistry, Van, Turkey

[2] Mersin University, Faculty of Pharmacy, Department of Biochemistry, Mersin, Turkey

[3] Mersin University, Faculty of Medicine, Department of Biophysics, Mersin, Turkey

INTRODUCTION:

The inhibition of adipocyte differentiation have a significant role on prevention of obesitiy and obesitiy-associated complications (1). To date, the inhibitory effect of numerous natural substances on adiposit differention have been investigated; however, a very small number of these substances have been reported to be capable of exhibiting a required level of inhibition (2). In this study, we aimed to detect whether punicalagin, substances found in pomegranate peel, are able to inhibit the conversion of pre-adiposits into mature adiposits.

MATERIALS AND METHODS:

3T3-L1 adipocyte precursor cells were stimulated so as to differentiate into mature adipocyte. Punicalagin solutions, with no cytotoxic effect, of varying concentrations of 2, 4, 6, 8 ve 10 μM were seperately applicated to differentiated 3T3-L1 cells. In all groups consisiting non-diffrentiated and differentianted cells that were applicated various concentrations of punicalagin, glyceraldehyde-3-phosphate dehydrogenase (GPDH) activity, Oil red O staining was performed to examine the cell morfology, and cellular trigliceride levels was measured spectrophotometrically. Furthermore, gene expressions of transcription factors (Peroxisome proliferator-activated receptor-γ (PPARγ), CCAAT-enhancer-binding proteins-α (C/EBPα) ve Sterol regulatory element-binding protein 1c (SREBP-1c)) were examined in order to investigate the effect of punicalagin on adipocyte differentiation.

RESULTS:

Although cellular trigliceride levels exhibited dose-related decrease, a statistical significance was not found ($p>0.05$). As a result of the morphological examination, punicalagin application caused a continuous decrease in cell size and cellular triglyceride accumulation. Despite the fact that GPDH activity decreased in all groups that were applicated punicalagin, this decrease was found to be statistically significant in groups that were applicated punicalagin at a concentration of 4-10 μM ($p<0.05$). The application of punicalagin at different concentrations showed a dose dependent lowering effect on expression of all three transcription genes. However, this decrease was found to be significant in groups that were applicated 6-10 μM punicalagin for PPARγ, 6-10 μM punicalagin for C/EBPα and 10 μM punicalagin for SREBP-1c ($p<0.05$).

CONCLUSIONS:

In line with these findings, it can be concluded that punicalagin was able to inhibit the adipocyte differentiation.

ACKNOWLEDGEMENTS:

This study was supported by the Research Fund of Mersin University in Turkey with Project Number: 2016-2-TP3-1891

REFERENCES:

1. Pope BD, Warren CR, Parker KK, Cowan CA (2016). Trends in Cell Biology, 8924:30048-30054. 2.Kulkarni AP, Mahal HS, Kapoor S, Aradhya SM (2007). Journal of Agricultural and Food Chemistry, 55:1491-1500.

OP-133: HISTOPATHOLOGICAL EFFECTS OF SILYMARIN IN THE LIVER TISSUES OF VANCOMYCIN-ADMINISTERED RATS

[1] Uckun, Z., [2] Kibar, D., [3] Guzel, S., [2] Bayrak, G.

[1]Mersin University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Mersin, Turkey

[2]Mersin University, Faculty of Pharmacy, Department of Histology and Embryology, Mersin, Turkey

[3]Mersin University, Faculty of Pharmacy, Department of Pharmacognosy, Mersin, Turkey

INTRODUCTION:

Silymarin (SLY) is a flavonolignan from the seeds of the milk thistle Silybum marinum L. (Asteraceae) and widely used as a hepatoprotective agent in the treatment of various liver disorders such as hepatitis, cirrhosis and fatty acid infiltration due to toxic chemicals and alcohol (1). Vancomycin (VCM) is a glycopeptide antibiotic and has an antibacterial action towards anaerobic and aerobic gram-positive bacteria (2). The present study aimed to evaluate histopathological effects of SLY in the liver tissues of VCM-administered rats.

MATERIALS AND METHODS:

Adult male Wistar albino rats were divided into seven groups; (i) Control group: saline was injected intraperitoneally (i.p.) at a dose of 0.5 ml/day, (ii) DMSO group: DMSO was injected at a dose 0.5 ml/day (i.p.), (iii) VCM group: VCM was injected i.p. at a dose of 400 mg/kg, (iv) SLY group: SLY dissolved in DMSO was injected intraperitoneally at a dose of 100 mg/kg, (v) VCM+SLY50 group: VCM and SLY was injected at a dose of 50 mg/kg i.p., (vi) VCM+SLY100: VCM and SLY was injected at a dose of 100 mg/kg i.p., (vii) VCM+SLY200 group: VCM and SLY was injected at a dose of 200 mg/kg i.p. The experiment was performed throughout 7 days for VCM group and 8 days for other groups. On 9th day, liver tissues were taken from tested animals under anesthesia. For light microscopic evaluation the tissues were fixed in formalin and processed by conventional method. They were stained with hematoxylin and eosin (H&E). For the histopathological examinations, sinusoidal dilatation, vacuolization, nuclear pleomorphism, necrosis, inflammation, picnosis and capsule thickening were evaluated and scored. Grading was applied as follows: (–) no meaningful histopathological damage; (+) mild degree of damage; (++) moderate degree of damage and (+++) severe degree of damage. Approval for the study was obtained from the Animal Experiments Local Ethics Committee in Mersin University.

RESULTS:

Histopathological changes were not detected in saline, DMSO and SLY100 groups. Besides, sinusoidal dilatation, vacuolization, nuclear pleomorphism were not observed at the corresponding groups. However, necrosis, inflammation, picnosis, capsule thickening were prominently observed in the liver tissues of rats treated with VCM. These alterations were significantly diminished in VCM+SLY50, VCM+SLY100, and VCM+SLY200 groups compared to VCM group.

CONCLUSIONS:

VCM administration cause some histopathologic changes in the liver tissues. The histopathological alterations can attenuate by administration of SLY.

ACKNOWLEDGEMENTS:

This study was supported by the Research Fund of Mersin University in Turkey with Project Number 2016-2-AP3-1906.

REFERENCES:

1. Kumas M, et al., (2018). Indian Journal of Experimental Biology, 56(3):158-163.
2. Basarslan F, et al., (2007). Human and Experiment Toxicology, 31(7): 726–733.

OP-134: INDOLE-DERIVED SPIROTHIAZOLIDINONES AS INHIBITORS OF INFLUENZA VIRUS FUSION

Cihan Ustundag, G.

Istanbul University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, İstanbul, Turkey

INTRODUCTION:

Seasonal influenza is a serious public health problem caused by influenza viruses which circulate in all parts of the world. To face the emerging resistance to presently available drugs, new anti-influenza drugs, preferably with different mechanisms of action, are needed (1). Targeting viral entry is an attractive antiviral strategy as it offers the advantage to combat viral pathogens at the very early steps of infection (2). Various compounds possessing spirothiazolidinone *moiety have been reported as hemagglutinin-mediated fusion inhibitors during the past years (3,4). On this basis, we have designed a series of compounds by the introduction of an indole ring into the spirothiazolidinone scaffold.*

MATERIALS AND METHODS:

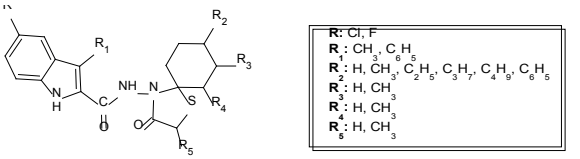
Indole-spirothiazolidinones were synthesized in five steps starting from aniline derivatives. The structures of obtained compounds were established by using spectroscopic and microanalytical data. Anti-influenza activity was evaluated in MDCK cells infected with influenza A and B viruses. The mechanism of action was elucidated by performing HA-mediated fusion (syncytium formation) assay.

RESULTS:

Some of the compounds exhibited significant and selective inhibitory effect on the replication of Influenza A/H3N2 virus at nanomolar concentrations. The inhibitory effect of the lead compound on syncytium formation indicated that compounds block hemagglutinin mediated membrane fusion.

CONCLUSIONS:

The promising anti-influenza A virus activity of indole-based spirothiazolidinone derivatives makes them interesting lead compounds for further anti-influenza drug development.



ACKNOWLEDGEMENTS:

This work was supported by the Research Fund of Istanbul University (Project Number T-20867 and 57695)

REFERENCES:

1. World Health Organization (WHO), Influenza (Seasonal) Fact Sheet. http://www.who.int/mediacentre/factsheets/fs211/en/ (accessed 30 January 2018).
2. Yang J et al. (2013). Viruses, 5:352-373.
3. Vanderlinden E et al., (2010). Journal of Virology, 84:4277-4288.
4. Göktaş F et al., (2012). Bioorganic & Medicinal Chemistry, 20:7155-7159.

OP-135: VOLTAMMETRIC DETERMINATION OF AN ANTIGUNGAL DRUG FROM PHARMACEUTICAL DOSAGE FORMS USING MODIFIED GLASSY CARBON ELECTRODES

Ozturk, G., Kul, D.

Karadeniz Technical University, Faculty of Pharmacy, Department of Analytical Chemistry, Trabzon, Turkey

INTRODUCTION:

Fungal infections which affects skin, hair, and nails are treated using antifungal medicines. Antifungal medicines can be found as topical, oral, intravenous, and intravaginal (1). Oral antifungals used commonly are fluconazole, itraconazole, ketoconazole, and terbinafine. The aim of this study to develop a sensitive determination method for terbinafine (TER) using voltammetry at polymer modified electrodes.

MATERIALS AND METHODS:

All experiments were achieved using a three-electrode electrochemical cell containing a glassy carbon (GC) working electrode, a platinum wire as counter electrode, and an Ag/AgCl electrode as reference. Polymer film modification was achieved using the procedure in the literature (2). All measurements were performed using an Autolab Pgstat128n potentiostat/galvanostat with Nova 1.10 software (Metrohm). Stock solution of TER (1x10-3 M) was prepared in deionized water. Phosphate (PB), Britton Robinson (BRB), and acetate (AcB) buffer solutions at different pH values were used.

RESULTS:

Electrochemical properties of TER were investigated on the anodic direction using cyclic (CV), differential pulse (DPV), and square wave (SWV) voltammetry methods, after the polymer film modification of GC electrode. The effect of pH on the redox process of TER was studied by CV. A well-defined anodic peak with the highest peak current was obtained in pH 3.5 AcB, thus, this buffer was selected for the further studies. Scan rate study with CV showed a diffusion controlled process under adsorption effect. The linearity range of the calibration graphs were determined as 0.04 - 20 μM (r = 0.997) for DPV with a detection limit of 0.008 μM. Finally, quantitative analysis of TER from its pharmaceutical dosage form was performed without any separation and filtration without the effect of the excipients.

CONCLUSIONS:

GC electrode was modified with polymer film and used for the determination of TER. Consequently, effective and economical modified electrode with high sensitivity and selectivity was obtained for the electrochemical analysis of TER.

REFERENCES:

1. Campoy S, Adrio JL (2017). Biochemical Pharmacology, 133:86-96.
2. Yang G, Yan J, Qi F, Sun C (2010). Electroanalysis, 22:2729-2738.

OP-136: THE EFFECTS OF IL-6 ON MMP-2 MRNA EXPRESSION IN MCF-7 BREAST ADENOCARCINOMA CELLS

Celik, A., Bakar Ates, F.

Ankara University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey

INTRODUCTION:

Cytokines are intracellular signalling molecules and they regulate the homeostasis of the immun system (1). Recently, the studies have been focused on the treatment of cancer by cytokines. Among these, interleukin-6 (IL-6) is identifed as a pleiotrophic cytokine and studies have shown many cellular functions of IL-6 in immune, hepatic, hematopoietic and neural cells (2). The studies have shown that IL6 expression has reduced in invasive breast tumors and inversely associated with histological tumor grade (3,4). There is little information about the role of IL-6 in breast cancer, so it's been suggested that IL-6 might be involved in regulating the growth of breast cancer cells. At present study we aimed to evaluate the effect of IL-6 on cell growth, apoptosis and MMP-2/-9 mRNA expression in MCF-7 breast carcinoma cells.

MATERIALS AND METHODS:

MCF-7 cells were treated with IL-6 in a concentration range between 10 – 100 nM and the cell growth were determined by MTT assay following a 24 hour of treatment. Apoptotic cell population was measured by annexin V binding assay and the mRNA expression levels of treated concentrations were performed by real-time PCR experiments.

RESULTS:

Our results showed a significant decrease in cell growth at 25, 50 and 100 nM IL-6 doses. The viable cell population was 85.111.86% in 25 nM treated group ($p=0.005$), whereas it has decreased to 70.044.85% at 100 nM treated group ($p<0.0001$). The results also showed that IL-6 has inducible efffect on apoptosis of MCF-7 cells. Real-time PCR

experiments have showed that IL6 has decreased MMP-9 mRNA expression at 100 nM concentration, whereas no significant decrease has been observed in MMP-2 expression.

CONCLUSIONS:

The present study has demonstrated that IL-6 has significant effects on cell growth and apoptosis of MCF-7 breast cancer cells. The inhibitory effect of IL-6 at MMP-9 expression suggests that IL-6 may prevent the metastasis of MCF-7 cells. Further studies are required to identify the underlying effects of IL-6 in cancer cells.

References

1. Lee S, Margolin K. (2011). Cancers (Basel), 3(4), 3856-3893.
2. Tamm et al., (1989) J. Exp. Med., 170: 1649-1669.
3. Fontanini et al., (1999). Br. J. Cancer, 80: 579-584.
4. Basolo et al., (1996). Cancer Res., 56: 3118-3122.

OP-137: EVALUATION OF TERATOGENIC EFFECTS OF CALCITRIOL TREATMENT IN PREGNANT WOMEN

[1] Cavusoglu, I., [1] Erkoseoglu, I., [1] Kadioglu, M., [2] Aran, T., [1] Kalyoncu, N.

[1]Karadeniz Technical University, Department of Pharmacology, Faculty of Medicine, Trabzon, Turkey

[2] Karadeniz Technical University, Department of Obstetrics and Gynaecology, Faculty of Medicine, Trabzon, Turkey

INTRODUCTION:

Calcitriol or 1,25-dihydroxycholecalciferol (abbreviated 1,25-(OH)2-D3) is the active form of vitamin D3. Calcitriol is used to treat hyperparathyroidism and hypocalcemia in people who have chronic kidney failure. It is also used to treat calcium deficiency in people with hypoparathyroidism. In terms of teratogenicity of calcitriol, some animal studies showed external and skeletal abnormalities. High doses (about 6 times the maximum human dose) is reported to show maternal mortality, decreased fetal weight, reduced newborn survival and hypercalcemia in the offspring. Hypercalcemia during pregnancy has been associated with suppression of parathyroid hormone in the neonate. This situation can lead to mental retardation and congenital aortic stenosis (1). There are no adequate controlled data on the use of calcitriol in pregnant women. In this study, we evaluated the outcomes of pregnant women used calcitriol.

MATERIALS AND METHODS:

22 pregnant women who were referred to Teratology Information Service (TIS) of Karadeniz Technical University, between 1999 and 2017 because of exposure to fetal calcitriol were evaluated. The age range of pregnant women was 22-40 years. Patient specific risk assessment and counseling were done. Data about the delivery information and fetal malformation were collected from hospital records and infants were followed up.

RESULTS:

Four cases lost follow-up were excluded. There were 13 healthy infants, 2 spontaneous abortus and 1 elective terminations among 18 pregnancies. One of healthy babies was premature. Elective termination was occurred at the 9th weeks of pregnancy because of the choice of family. One baby had hyperthyroidism. Unilateral renal agenesis was found in one case in terms of major malformations. Maternal characteristics of women who used calcitriol during pregnancy and outcomes excluding healthy and inaccessible cases are shown in Table 1.

Table 1. Maternal characteristics of women used calcitriol during pregnancy and outcomes excluding healthy and inaccessible cases

Age	Periods (weeks)	Additional drugs	Other risk factors	Risks	Results
37	0-5	Calcium besylate, magnesium citrate, naproxen sodium, amitriptyline	Maternal age	Low	Hyperthyroidism
34	3-4	Allopurinol, ferrous sulphate, amlodipine	-	High	Spontaneous abortus (at 8th weeks of gestation)
32	0-6	Telmisartan	-	High	Spontaneous abortus (at 10th weeks of gestation)
36	0-8	Levothyroxine sodium, paroxetine	Maternal age	Low	Elective termination (at 9th weeks of gestation)
34	0-6	Alendronate sodium, acemetacin, vitamin D, calcium carbonate+calcium lactate gluconate	-	High	Unilateral renal agenesis

CONCLUSIONS:

The outcome of exposure to calcitriol in the first trimester of pregnancy in our case series resulted with an anomaly (renal agenesis). However, it is difficult to attribute these anomaly to calcitriol because of the limited numbers of cases. Further studies are clearly needed to confirm the safety of calcitriol in the pregnancy.

REFERENCES:

1. Krysiak R, Kobielusz Gembala I, et al., (2011). Hypoparathyroidism in pregnancy. Gynecol Endocrinol. 2011;27:529-532. Epub 2011 Apr 5.

OP-138: SYNTHESIS AND DETERMINATION OF POTENTIAL BIOLOGICALLY ACTIVE SOME NEW N'-(SUBSTITUTED BENZYLIDENE)-2,2-BIS(SUBSTITUTED PHENYL)-2-HYDROXYACETOHYDRAZIDE DERIVATIVE COMPOUNDS

[1] Dogan, IS., [1] Kayiki, N., [1] Sellitepe, HE., [2] Yayli, N.

[1] Karadeniz Technical University, Department of Pharmaceutical Chemistry, Trabzon, Turkey

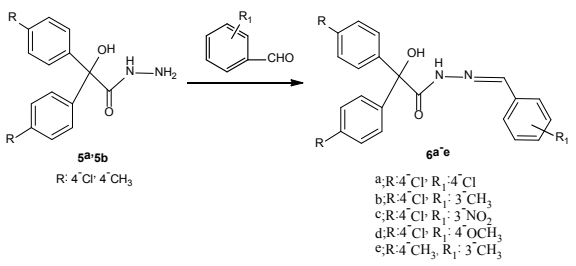
[2] Karadeniz Technical University, Department of Pharmacognosy, Trabzon, Turkey

INTRODUCTION:

The hydrazide-hydrazone derivatives are noted for their ability for ring closure and suitable for substitution (1,2).The compounds obtained are known to exhibit activities such as antituberculer, antimicrobacterial, antitumoral, anticancer (3,4). In this work, the synthesis of biologically active hydrazide-hydrazone derivatives was aimed and 5 novel N'-(substitutedbenzylidene)-2,2-bis(substituted phenyl)-2-hydroxyacetohydrazide compounds were synthesized.

MATERIALS AND METHODS:

4,4'-bis(substituted)benzoin derivative compounds 1a,b were obtained by the reaction of potassium cyanide with p-substituted benzaldehyde (5) and 4,4'-bis (substituted)benzyl derivative compounds 2a,b were obtained by reaction of compounds 1a,b with concentrated nitric acid (6). 2,2-bis(substituted phenyl)-2-hydroxyacetic acid derivative compounds 3a,b were obtained by the reaction of compounds 2a,b in a potassium hydroxide medium. Methyl 2,2-bis(substituted phenyl)-2-hydroxyacetate derivative compounds 4a,b have been obtained according to the Fischer esterification reaction (7). Reaction of the compounds 4a,b with hydrazine hydrate gave the resulting hydrazide derivative compound 5a,b and its reaction with the appropriate substituted benzenaldehyde derivatives gave the resultant compounds 6a-e (3,4 (Scheme 1). This reaction chain resulted in the synthesis of 5 new N'-(substituted benzylidene)-2,2-bis(substituted phenyl)-2-hydroxyacetohydrazide derivative compounds.



Scheme 1. Synthesis of new biologically active hydrazone derivatives

RESULTS:

Structures of synthesized 5 new compounds were identified by spectroscopic methods such as IR, 1H-NMR, 13C-NMR and mass.

CONCLUSIONS:

The acetylcholinesterase enzyme inhibition and anticancer activities of the compounds have begun to be studied.

REFERENCES:

1. Kovalenko SI et al., (2013). SciPharm,81,359–391.
2. Andrade CH et al., (2008). Mol Divers,12,47–59.
3. Alam MS et al., (2017). Bioorganic & Medicinal Chemistry, 25,389–396.
4. Taha M et al., (2017). Chinese Chemical Letters, 28,607–611.
5. Ling H et al., (2013). Applied Chemical Industry, 42(7),1281-3.
6. Acharjee J et al., (2015). World J.of Pharm. and Pharmaceutical Sci., 4(06),1741-9.
7. Dawar P et al., (2014) Synthetic Communications, 44(6),836-846.

OP-139: SYNTHESIS, ANTIMICROBIAL ACTIVITY AND ELECTROCHEMICAL BEHAVIOUR OF ALKYL 4-(4-(3-METHOXYCARBONYL)-2,6,6-TRIMETHYL-5-OXO-1,4,5,6,7,8-HEXAHYDROQUINOLINE-4-YL) PHENYL)-6,6-DIMETHYL-5-OXO-1,4,5,6,7,8-HEXAHYDROQUINOLINE-2-CARBOXYLATE

[1] Celik, H., [1] Eroglu, A., [2] Baymak, MS., [3] Cetin, G., [3] Simsek, R., [3] Safak, C.

[1]Yeditepe University, Department of Analytical Chemistry, Istanbul, Turkey

[2]Marmara University, Department of Chemistry, Istanbul, Turkey

[3]Hacettepe University, Department of Pharmaceutical Chemistry, Ankara, Turkey

INTRODUCTION:

1,4-Dihydropyridine (1,4-DHP) derivatives are classified as calcium channel modulators and have vasodilator, antihypertensive, bronchodilator, antiatherosclerotic, antitumor, antimutagenic, hepatoprotective, geroprotective, antidiabetic, antiinflammatory, antiallergic, neurotropic, antibacterial, antimicrobial, antioxidant and analgesic activities (1,2). Studies on the antibacterial and antifungal activity of the compounds obtained by condensing dialdehydes with various ring systems containing nitrogen atoms are continuing (3). In view of the mentioned findings, we have some effort to identify new molecules that may be valuable in designing new, active and less toxic antimicrobial agents. In this study we have used dialdehyde compounds to synthesize

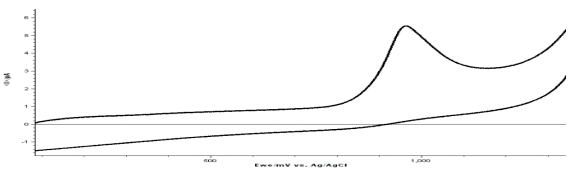
new condensed 1,4-DHP derivatives. The structure of the compounds was proven with instrumental techniques. The antibacterial and antifungal activities of the synthesized compounds were realized. Electrochemical behaviour of the compounds was determined and correlated with biological activity.

MATERIALS AND METHODS:

In this study, the electrochemical behavior of studied compounds have been investigated by using cyclic voltammetry and polarography. Simple buffer systems were used with pH values between 1 and 12 and the chemicals used to prepare these buffer solutions were of analytical grade.

RESULTS:

In this study, 5 new alkyl 4-(4-(3-methoxycarbonyl)-2,6,6-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-4-yl)phenyl)-6,6-dimethyl-5-oxo-1,4,5,6,7,8-hexahydro quinoline-2-carboxylate derivatives (RGs) synthesized via a modified Hantzsch reaction. The structure of the compounds were elucidated by using spectral methods. The synthesized compounds were subjected to in vitro antibacterial and antifungal studies. In the electrochemical part, oxidation mechanism was elucidated by using cyclic voltammetry (see Figure) with a glassy carbon electrode in aqueous buffer solution pH between 1 and 12. It was observed that peak potentials were function of acidity of the solution. Electrooxidation mechanism is suggested based on experimental data. Further studies on electrochemical reduction mechanism are currently under investigation.



CONCLUSION:

Electrochemical behavior of above mentioned compounds has been elucidated by using cyclic voltammetry and DC polarography.

REFERENCES:

1. Yıldırım SO, Buyukmumcu Z, Butcher RJ, Cetin G, Simsek R, Safak C (2018). J of Molecular Structure, 1163:161-166.
2. Baydar E, Gunduz MG, Krishna VS, Simsek R, Sriram D, Yildirim SO, Butcher RJ, Safak C (2017). Res. Chem. Intermediates, 43(129): 7471-7489.
3. Khanmohammadi H, Abnosi MH, Hosseinzadeh A, Erfantalab M (2008). Spectrochimica Acta Part A: molecular and Biomolecular Spectroscopy, 71(4): 1474-1480.

OP-140: PHENOTHIAZINE-STRUCTURED COMPOUNDS HAVE DIFFERENT EFFECTS ON SECRETASES WITH THERAPEUTIC POTENTIAL IN ALZHEIMER'S DISEASE

Yuksel M., Tacal O.

[1] Hacettepe University, Department of Biochemistry, School of Pharmacy, Ankara, Turkey

INTRODUCTION:

According to the amyloid hypothesis, the accumulation of the amyloid-β (Aβ) peptides in protein aggregates causes various pathological changes, ultimately leading to neurodegeneration and dementia. The formation of Aβ peptides is a consequence of the processing of amyloid precursor protein (APP) via the amyloidogenic pathway, in which APP is successively cleaved by β- and γ-secretases while α-secretase is responsible for the formation of sAPPα and C83 fragment through the non-amyloidogenic pathway (1). These major secretases involved in the processing of APP are the enzymes with therapeutic potentials in Alzheimer's disease (AD) (2). Our earlier studies showed that two phenothiazine compounds with potent anti-cholinesterase activities (3), toluidine blue O (TBO) and thionine (TH), ameliorate amyloid metabolism by decreasing Aβ levels secreted by PS70 cells in a dose-dependent manner (4). In the present study, we tested whether TBO and TH show these mitigating effects by targeting the secretases involved in APP processing.

MATERIALS AND METHODS:

We treated Chinese hamster ovary cells overexpressing human wild type APP751 and PSEN1, namely PS70 cells, with 0-15 μM TBO or TH for 6-24 hours. After treatment, the levels of PSEN1 (γ-secretase) and ADAM10 (α-secretase) were analyzed in PS70 cell lysates by Western blot.

RESULTS:

Our results showed that both TBO and TH reduced the levels of PSEN1 in a dose-dependent manner significantly. On the other hand, the compounds had reverse effects on the levels of ADAM10. While 15 μM TBO decreased the levels of ADAM10 by 33% (*, $p<.05$), 15 μM TH caused almost 90% increase (***, $p<.001$) when compared to control.

CONCLUSIONS:

Overall, these preliminary results suggest that TBO and TH may be AD therapeutic candidates targeting secretases as well as the cholinergic system.

REFERENCES:

1. Hardy J., Selkoe DJ,(2002). Science, 297:353-356.
2. De Strooper et al., (2010). Nature Reviews Neurology, 6:99-107.

3. Biberoglu et al., (2016). *Archives of Biochemistry and Biophysics.,* 604:57-62.
4. Yuksel et al., (2017). Biochimie, 138:82-89.

OP-141: MOLECULAR MODELLING OF THE ANTICONVULSANT ACTIVITY OF 1-PHENYL/1-(4-CHLOROPHENYL)-2-(1H-1,2,4-TRIAZOL-1-YL)ETHANOL ESTERS

[1] Sari, S., [2] Dogan, IS., [3] Ozdemir, Z., [3] Bozbey, İ., [3] Karakurt, A., [1] Sarac, S.

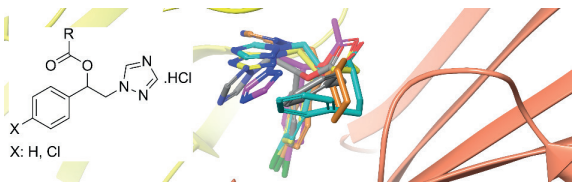
[1] Hacettepe University, Department of Pharmaceutical Chemistry, Ankara, Turkey

[2] Karadeniz Technical University, Department of Pharmaceutical Chemistry, Trabzon, Turkey

[3] Inonu University, Department of Pharmaceutical Chemistry, Malatya, Turkey

INTRODUCTION:

(Arylalkyl)azoles are a class of antiepileptic compounds known for nafimidone, denzimol, and loreclezole (1). Potent anticonvulsant activity of some 1-phenyl/1-(4-chlorophenyl)-2-(1H-triazol-1-yl)ethanol esters was previously determined (2). In this study we modelled their ADMET properties and possible anticonvulsant mechanisms.



MATERIALS AND METHODS:

The compounds were modelled and minimized using MacroModel (Schrödinger, LLC, NY, 2018), PRCG method, and OPLS_2005 force field. Their physicochemical and pharmacokinetic properties were calculated using QikProp. The GABAAR homology model obtained from the study of Bergmann et al. (3) was prepared for docking by the Protein Preparation Wizard of Maestro (Schrödinger, LLC, NY, 2018) where the ionization states and proton orientations were set. Ligands were docked to the benzodiazepine (BZD) binding site by Glide at extra precision mode (4).

RESULTS:

QikProp results show that the active compounds are drug like and have favorable pharmacokinetics. Docking simulations predicted high affinity binding to the BZD binding site of the GABAAR model with interactions in line with biological and theoretical data (3).

CONCLUSIONS:

1-Phenyl/1-(4-chlorophenyl)-2-(1H-1,2,4-triazol-1-yl)ethanol esters were identified as promising anticonvulsant compounds with predictably good ADMET properties. Their anticonvulsant action might be the result of BZD-type activation of GABAAR.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG 114S862).

REFERENCES:

1. Dalkara S, Karakurt A (2012). Current Topics in Medicinal Chemistry, 12:1033-1071.
2. Doğan İS et al., International Multidisciplinary Symposium on Drug Research and Development, 5-7 October 2017, Erzurum, Turkey.
3. Bergmann R, et al., (2013). PLoS One, 8(1): e52323.
4. Friesner RA, et al., (2006). Journal of Medicinal Chemistry, 49:6177–6196.

OP-142: A HIGHLY SENSITIVE ELECTROCHEMICAL NANOBIOSENSOR FOR THE ANALYSIS OF PRANGOS MELIOCARPOIDES AND DNA INTERACTION

[1,2] Subak, H., [3] Dalar, A., [1] Ozkan Ariksoysal, D.

[1]Ege University, Faculty of Pharmacy, Analytical Chemistry Department, Izmir, Turkey

[2]Yuzuncu Yil University, Faculty of Pharmacy, Analytical Chemistry Department, Van, Turkey

[3]Yuzuncu Yil University, Faculty of Pharmacy, Pharmaceutical Botany Department, Van, Turkey

INTRODUCTION:

Prangos meliocarpoides boiss. Var. Meliocarpoides belong to Appiaceae is an endemic plant taxa which has been used as food and medicine in eastern Anatolia. The extract obtain from this plant has pronounced capacity of oxygen radical suppression. The effect of the extract on the oxygen radicals are still being investigated in continuing studies. The subject of “nanoparticle (NP) modified electrodes” with their excellent features of such as enhanced surface area, good conductivity and biocompatibility have still been under investigation (1-3). NPs not only provide a suitable environment for biomaterial modification, but also improve the detection limit of biosensors. In this study, the metal NPs modified biosensor was developed for the detection of the plant extract-DNA interaction based on guanine/adenine signal. There is no report about Prangos meliocarpoides and DNA interaction by using metal NP immobilized pencil graphite electrode (PGE) in the literature.

MATERIALS AND METHODS:

NPs modification was tested with cyclic voltammetry by PGE. The change in the oxidation signal of guanine (+1.0 V) or the extract (+0.36V) were measured by using differential pulse voltammetry (DPV) via AUTOLAB 12 potatiostat/galvanostat device.

RESULTS:

The interaction type of the extract with DNA was studied with bare or nanomaterial modified PGE and some optimum detection parameters were determined. The nanoparticle modification was found to increase the electrode conductivity and DNA binding capacity by nearly 3-fold.

CONCLUSIONS:

Newly-developed biosensor could be used for the rapid, cost effective and highly sensitive detection of plant extract–DNA interaction as a powerful alternative method for investigating the effects of medicinal plants on DNA.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Ege University Project Coordination Center (16ECZ/033).

REFERENCES:

1. Wang J (2005). Analyst, 130:421-426.
2. Agui L, Yanez Sedeno P, Pingarron JM (2008). Anal. Chim. Acta, 622:11–47.
3. Ozkan Ariksoysal D et al., (2017). Talanta,166:27–35.

OP-143: ANTICANCER AND ANTI-INFLAMMATORY ACTIVITIES OF EDIBLE MUSHROOM HYDNUM REPANDUM

[1] Shomali N., [1] Onar O., [1] Akata I.,[1] Yildirim O.

Ankara University, Faculty of Science, Department of Biology, Ankara, Turkey

INTRODUCTION:

Mushrooms are one of the most important food sources for humanity, with a large number of edible species with different nutritional values and they also naturally contains a wide range of biologically active compounds. Nowadays there is a growing interest in the therapeutic use of bioactive metabolites derived from natural products. These bioactive components are defined as natural sources of antioxidant, antitumor, antiviral, antimicrobial and immunomodulatory agents. In this study, we investigated the ethanolic extract of an edible mushroom Hydnum repandum to find a new bioactive agent with anti-inflammatory and anticancer activities.

MATERIALS AND METHODS:

The mushroom material was obtained from the bazaar of the Black Sea region and analyzed for the flavonoids and phenolic compound content. The antioxidant capacity of the extract was determined by DPPH method. Its effect on aldose reductase activity was examined by the kinetic assay. Furthermore, extract-induced cell growth inhibition was performed in two different human cell lines (colorectal and breast) using the MTT assay.

RESULTS:

Total phenolic and flavonoid content of the ethanolic extract of H. repandum was determined as 3.30 ± 0.0016 mg GAE/g and 2.547± 0.0016 QE/g values, respectively. DPPH radical scavenging capacity was determined as 35% and aldose reductase enzyme activity was effectively inhibited as 45%. Also, H. repandum extract induced the cell growth inhibition of HT-29 cells as 16% and MCF-7 cells as 30% at the 500 µg/mL final concentration.

CONCLUSIONS:

Aldose reductase plays important role in the cellular oxidative defense. In addition, some studies show that inhibition of Aldose reductase can prevent colon cancer (1). Therefore, new therapeutic methods for the colon cancer can be developed by investigating the ability of H. repandum to inhibit aldose reductase.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (116Z125)

REFERENCES:

1. Tammali R, Srivastava SK, Ramana KV (2011). Curr Cancer Drug Targets, 11:560-71.

OP-144: A NOVEL OXIDATIVE PRETREATED PENCIL GRAPHITE BASED PARACETAMOL SENSOR: PREPARATION, CHARACTERIZATON AND APPLICATION TO TABLET ANALYSIS

Keskin, E., Erturk, AS

Adiyaman University, Department of Analytical Chemistry, Faculty of Pharmacy, Adiyaman, Turkey

INTRODUCTION:

Analytical assay and quality control of paracetamol (PAR), N-acetyl-p-aminophenol or acetaminophen, are of great importance as its one of the most frequently used analgesics and antipyretics (1). Overdose of PAR can cause serious harms in liver and kidney (2). Therefore, there has been a growing interest towards developing simple, rapid, sensitive and selective methods for the detection and quantification of PAR in biological samples and pharmaceuticals (3).

MATERIALS AND METHODS:

Surface morphology of the OP-PGE was characterized by scanning electron microscopy (SEM) and attenuated total reflectance Fourier-transform infrared spectroscopy (ATR-FTIR). Electrochemical behavior of PAR on the OP-PGE was investigated with cyclic voltammetry (CV) and electrochemical impedance spectroscopy (EIS). Measurements were performed by adsorptive stripping voltammetry (AdSWV).

RESULTS:

Under optimized experimental conditions, the linear dynamic range of calibration was between 0.052-2.85 μM with a detection limit of 18.4 nM (S/N=3). The OP-PGE showed a good sensitivity, selectivity, and stability compared to the bare PGE. The developed oxidative pretreated PGE (OP-PGE) sensor was used for the first time to determine PAR from pure and commercial tablet dosage forms.

CONCLUSIONS:

Results revealed that the OP-PGE could successfully determine PAR from the tablets with no tedious electrode fabrication and sample pretreatment methods, and in situ oxidative pretreatment could be an alternative, simple and sensitive approach for the fabrication of PGE based electrodes to use them in the pharmaceutical analysis in the future studies.

ACKNOWLEDGEMENTS:

This study was supported by Adiyaman University Scientific Research Projects Coordination Department (Project Number: ECZFMAP/2018-0001).

REFERENCES:

1. Bosch ME, Sánchez AJR, Rojas FS, Ojeda CB (2006). Journal of Pharmaceutical and Biomedical Analysis, 42(3):291-321.
2. Saraswathyamma B et al., (2008). Electroanalysis, 20(21):2317-2323.
3. Esteve Romero J, Albiol Chiva J, Peris Vicente J (2016). Analytica Chimica Acta, 926:1-16.

OP-145: ENHANCEMENT OF YAMANAKA FACTORS EFFECIENCY BY USING AXOLOTL OOCYTES

[1] Bereketoglu S., [2] Alberio R., [3] Johnson A.

[1] Ankara University, Faculty of Science, Department of Biology, Ankara, Turkey

[2] The University of Nottingham, School of Biosciences, Nottingham, UK

[3] The University of Nottingham, School of Life Sciences, Institute of Genetics, Nottingham, UK

INTRODUCTION:

Reprogramming of somatic cells requires a complex mechanism in which chromatin environment alters by epigenetic remodelling and reactivating pluripotency genes (1, 2). Yamanaka factors, Klf4, c-Myc, Oct4 and Sox2, induce pluripotency in differentiated cells to generate induced pluripotent cells (iPSCs) (2). However, previous studies showed that epigenetic inheretance of iPSCs is a limiting factor to establish pluripotency (3). Reprogramming of differentiated cells by using Axolotl oocyte extract (AOE) can reactivate the Nanog gene in mammalian cells, 'the gateway to the pluripotent ground state' (4, 5). In this study, we aimed to accelerate the efficiency of Yamanaka factors by using the capacity of Axolotl oocytes to remodel epigenetic pattern of somatic chromatin by providing AxNanog, an ortholog of mammalian Nanog.

MATERIALS AND METHODS:

Inducible NIH3T3 cell line expressing Oct4 and Sox2 was generated and treated with AOE for 6 hours. ChIP was carried out using Oct4 antibody and Oct4-bound immunoprecipitated DNA was analysed by qPCR for the regulatory regions of the mouse Nanog gene.

RESULTS:

We first showed that AOE is capable of remodelling the epigenetic environment in the mammalian chromatin. Then, we demonstrated that endogenous Oct4/Sox2 expression procure around 2 fold increase on the Oct4 binding on the mouse Nanog promoter and enhancer while AOE can enhance this binding to about 14 fold. This suggests that the factors AOE contains prepare the epigenetic profile of the somatic chromatin and make the regulatory regions of pluripotency genes more accessible to Oct4.

CONCLUSIONS:

This study clarifies that the efficiency of iPSCs can be enhanced by reducing the effects of epigenetic memory in somatic chromatin by using Axolotl oocytes, which provides AxNanog. Further experiments are still required to use this synergy between iPSCs and Axolotl oocyte in therapeutics.

ACKNOWLEDGMENTS

This study was supported by a grant of Republic of Turkey Ministery of National Education.

REFERENCES:

1. Simonsson S, Gurdon J (2004). Nature Cell Biology, 6: 984-990.
2. Takahashi K, Yamanaka S (2006). Cell, 126:663-76.
3. Halley-Stott RP, Gurdon (2013). Briefings in Functional Genomics, 12: 164-173.
4. Dixon et al., (2010). Development, 137(18):2973-80.
5. Silva et al. (2009). Cell, 138(4): 722-37.

OP-146: ELECTROCHEMICAL CHARACTERIZATION OF VARIOUS BY SUBSTITUTED PERYLENE DIIMIDE LIGANDS AND THEIR PLATINUM(II) AND PALLADIUM(II)-2,2′:6′,2″-TERPYRIDYL COMPLEX IONS

[1] Orman, EB., [2] Buyukeksi, SI., [2] Sengül, A., [1] Ozkaya, AR.

[1]Marmara University, Department of Chemistry, Istanbul, Turkey

[2]Bülent Ecevit University, Department of Chemistry, Zonguldak, Turkey

INTRODUCTION:

Macrocyclic compounds involving conjugated p-electron sytems usually display reversible electron transfer processes at modest potentials and thus, good chromophore, electron acceptor/donor and conducting properties. Due to their mentioned properties, these compounds have potential for usage in various electrochemical systems, for instance in electrochromic devices (1, 2). In this study, electrochemical, spectroelectrochemical and electrochromic characterization of various bay-substituted perylene diimide (PDI) ligands and their platinum(II) and palladium(II)-2,2′:6′,2″-terpyridyl complexes have been performed in solution medium. In addition, electrochromic measurements for the cast films of a group of PDI compounds on indium tin oxide (ITO) were performed.

MATERIALS AND METHODS:

Cyclic voltammetry (CV), square wave voltammetry (SWV), in-situ spectroelectrochemical (SEC) and spectrochronoamperometric (SCA) measurements were carried out both in solution and in the film environment.

RESULTS:

It is clear from the electrochemical redox potentials of PDI compounds that these compounds are reduced easily and thus, can be used as electron acceptors in the construction of new optoelectronic devices.

CONCLUSIONS:

The compounds displayed enriched redox properties with low HOMO-LUMO band gaps. Also, the cast film of the platinum complex of pyridine substituted perylene diimide ligand on ITO glass illustrated a distinct color transition between blue and turquoise.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (Project No: 214Z090)

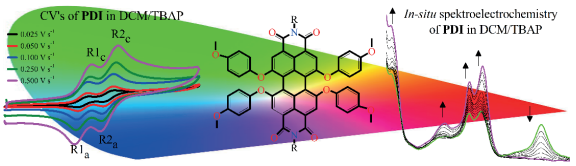


Fig.1 Cyclic waves and in-situ spectral changes of PDI

REFERENCES:

1. Buyukeksi SI, Orman EB, Sengul A, Altindal A, Ozkaya AR (2017). Dyes and Pigments, 144:190-202.
2. Buyukeksi SI, Sengul A, Erdonmez S, Altindal A, Orman EB, Ozkaya AR (2018). Dalton Transactions, 47:2549-2560.

OP-147: IN VITRO ANTIPLATELET STUDIES ON VIRTUALLY DISCOVERED GPVI DRUG CANDIDATES

[1] Olgac S., [2,3] Olgac A., [1] Ozkan, Y.

[1] Gazi University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey

[2] Gazi University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

[3] Evias Pharmaceutical R&D Ltd., Gazi Teknopark G1-101, Ankara, Turkey

INTRODUCTION:

Platelet activation is essential for hemostasis, however uncontrolled and excessive platelet activation and aggregation are harmful for the health (1). Therefore, new drugs without bleeding risk and preventing undesired plug formation are needed.

MATERIALS AND METHODS:

Marketed drugs, aiming to drug repurposing, and Molport compounds, a library of in stock and ready to order chemical compounds, were used to discover novel Glycoprotein VI (GPVI) receptor inhibitors. After physicochemical filters, lead compounds were chosen to test their in vitro antiplatelet activities. Platelet aggregation was measured by using an aggregometer according to the turbidimetric method described by Born et. al. (2). In vitro aggregation studies were performed with collagen, thrombin and arachidonic acid as inducers in washed platelets.

RESULTS:

16 Molport compounds and 8 marketed drugs, chosen by an e-pharmacophore model which is designed from GPVI receptor antagonists, were tested in vitro. Moreover, the molecules' docking scores, structural interactions and positions of binding to GPVI were taken into consideration while choosing the compounds. All compounds tested both at 1 mM and 100 µM against various platelet agonists. Molport compounds at 100 µM significantly showed inhibitor activities on platelet aggregation induced with

collagen (Z16043060; 88.17±1.78, AE641/05538014; 79.69±2.78, STK763609; 76.12±2.43), whereas they did not show any significant inhibition at 100 µM against thrombin induced platelet aggregation (Z16043060; 0.51±0.89, AE641/05538014; 0.00±0.00, STK763609; 6.79±2.05).

CONCLUSIONS:

Results imply that some tested compounds may have inhibitory activity against to GPVI. Our studies in which convulxin is used as GPVI-selective agonist have been going on to be able to find whether the active compounds specific to GPVI receptor.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (216S637)

REFERENCES:

1. Andrews R, Arthur J, Gardiner E (2014). Journal of Blood Medicine, 5:59–68.
2. Born G, Cross M (1963). Journal of Physiology, 168:178-195.

OP-148: DETERMINATION OF ACIDITY CONSTANTS AND THERMODYNAMIC PROPERTIES OF STATINS

Bakirhan, NK

Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

Hitit University, Faculty of Science and Art, Department of Chemistry, Corum, Turkey

INTRODUCTION:

Statins are primarily the most therapeutically effective drugs which reduce LDL cholesterol and triglyceride levels in the bloodstream of patients at risk of cardiovascular disease. Statins can lower cholesterol by 20 to 60%. Their water solubility depends to their chemical structures which affect their metabolism, distribution, absorption and excretion. Most drugs have ionization sites that can be protonated or deprotonated at different pH values. Hence, the pharmacodynamics and pharmacokinetic properties of drugs can be very important. The acidity constant value may be helpful in predicting the behavior of a drug under in vivo conditions. Various analytical methods have been used for the determination of acidity constants such as spectrometry, potentiometry and chromatography. Up to date, there is no publish study about determination of acidity constants for rosuvastatine by electrochemical methods. These methods have excellent features such as rapid, precise, cheap and do not require pretreatments. In this study, voltammetry and electrochemical impedance spectroscopy methods have been applied to investigation of acidity constants and thermodynamic parameters of statins in aqueous mediums.

MATERIALS AND METHODS:

Electrochemical experiments were performed by cyclic voltammetry and electrochemical impedance spectroscopy. Current-voltage curves were recorded by using Palmsens 5.2. Pyrolytic graphite electrode (BASi; ø: 3 mm, diameter) was used as working electrode, platinium as counter and Ag/AgCl (BASi; 3 M KCl) used as reference electrode. pH effect study was applied between pH 2.0-11.0 Britton-Robinson buffers (0.04 M). Rosuvastatine stock solution (1×10-3 M) was prepared with methanol. In measurement solution, it was fixed to 10% ratio. 0.01 M sodium dodecylsulphate solution (1 mL) was added to measurement solution.

RESULTS:

Dissociation constant of the basic drug rosuvastatine was found by using cyclic voltammetry and electrochemical impedance spectroscopy. pKa value of rosuvastatine calcium was obtained as 3.8 and 3.9 by CV and EIS methods, respectively. The obtained pKa value is in close agreement with reported in the literature. ΔG, ΔH and ΔS parameters were calculated.

CONCLUSIONS:

This work shows that electrochemical methods are reliable and simple for pKa detection of drugs.

OP-149: ANALYSIS OF POSITIVE EFFECTS OF TWO LACTOBACILLUS STRAIN IN MICE FED HIGH FAT DIET

[1] Ivanović, N., [1] Đorđević, B., [2] Minić, R., [3] Michaličková, D.

[1] Faculty of Pharmacy, Department of Bromatology, Belgrade, Serbia

[2] Institut of virology, vaccines and sera "Torlak", Belgrade, Serbia

[3] First Faculty of Medicine, Department of Farmacology, Prague, Czech Republic

INTRODUCTION:

Modern lifestyle has been responsible for the increased incidence of obesity and obesity-induced comorbidities in modern age (1). High fat diet induces similar changes in mice. These changes can be ameliorated by the administration of some Lactobacillus species (2,3). The aim of this study was to evaluate positive effects of two Lactobacillus strains on high fat diet induced pathology in mice and durability of these effects upon the 8 weeks wash out period.

MATERIALS AND METHODS:

Mice on high fat diet were given Lactobacillus plantarum WCFS1 or Lactobacillus rhamnosus LA68 for three months followed by a two month wash out period. Mouse sera was collected and various parameters analyzed.

RESULTS:

After 16 weeks of HFD regime, in experimental group on HFD regime alone there was a significant increase in weight and liver steatosis developed. This was accompanied by increased levels of blood lipids and increased leptin levels. Administration of WCFS1 strain in HFD regime prevented the increase in mice body weight and led to a significant decrease in serum triglycerides and LDL cholesterol. The administration of LA68 also resulted in significantly lower body weight of the animals, led to a significant decrease in serum total and HDL cholesterol. Upon the 8 weeks wash out period the only remaining beneficial effect was significantly lower mouse weight in the supplemented groups compared to the HFD group.

CONCLUSIONS:

Active probiotic administration of two Lactobacillus species/strains had positive influence on metabolic parameters in mice on HFD regime, but these positive outcomes were short term after ending probiotic administration.

REFERENCES:

1. Lombardo et al., (2016). Front Endocrinol (Lausanne), 7: 49.
2. Kim et al., (2013). Biochem Biophys Res Commun., 431(2): 258-63.
3. Yoo et al., (2013). Obesity (Silver Spring), 21(12): 2571-8.

POSTER PRESENTATIONS

P-001: THE EFFECT OF LED ILLUMINATION ON METABOLIC PROFILE OF MEDICINAL PLANTS IN VITRO CULTURES

[1] Kozłowska, W., [1] Zielińska, S., [2] Bohater, A., [2] Chmara, S., [2] Grzelka, K.,[2] Kostyrka, K., [2] Niewiadomski, M., [2] Smakosz, A., [2] Treter, N., [3] Libik, M., [4] Kolniak Ostek, J., [4] Oszmiański, J., [5] Sowa, I., [5] Wójciak Kosior, M., [6] Matkowski, A.

[1]Wroclaw Medical University, Department of Pharmaceutical Biology, Poland

[2]Student's Research Society, Group K76 - Pharmaceutical Botany

[3]Institute of Plant Physiology, PAS, Krakow, Poland

4Wroclaw University of Life Sciences, Department of Fruits, Vegetables and Nutraceuticals, Poland

5Lublin Medical University, Department of Analytical Chemistry, Poland

6Botanical Garden of Medicinal Plants, Wroclaw, Poland

INTRODUCTION:

Cell, tissue, and organ cultures of medicinal plants proved to be essential for the discovery of biosynthetic pathways and their regulation, providing means for influencing pharmacologically relevant natural products. In the present study, we used in vitro cultures of several medicinal plants (Agastache rugosa, Salvia yangii, Moluccella laevis, Chelidonium majus, Stevia rebaudiana) to test the influence of different illumination regimes and media composition on morphogenesis and bioactive metabolite contents.

MATERIALS AND METHODS:

Tissue and organ cultures were initiated from explants obtained from various organs of aseptically germinated seedlings. Callus tissue was induced on various media based on Murashige and Skoog salts supplemented with a combination of auxins - IAA, NAA, 2,4-D and cytokinins - BAP and kinetin. Microshoot cultures were obtained from excised apices placed on shoot multiplication medium. The cultures were maintained in different illumination regimes - white fluorescent and LED of various spectra. Phytochemical screening was performed using spectrophotometry and HPLC.

RESULTS:

The morphogenic response of explants differed between white and photosynthetically active radiation (PAR) light. Callus induction percent, number and length of axillary shoots, rooting and biomass increase was among the parameters that were determined. Conditions of culture, including illumination spectrum, influenced content of rosmarinic acid and isoquinoline alkaloids significantly. However, response to each of the tested factor differed between species. Precursor (amino acids) feeding influenced developmental processes but did not increase level of the respective metabolites. Surprisingly, feeding resulted in marked decrease of alkaloid production in vitro in Chelidonium.

CONCLUSIONS:

The spectrum of light illuminating plant in vitro cultures can influence morphogenic processes and accumulation of specialized metabolites that are important for pharmacological properties. However, each species reacts differently and to improve accumulation of desired substances, the conditions of culture must be established experimentally.

ACKNOWLEDGEMENTS:

This study was supported by grants of WMU D030.17.028, ST.D030.15.043 and of MNiSW SPUB grant for the Botanical Garden.

P-002: EVALUATION OF DRUGS SOLD UNDER THE NAME OF GÜL (ROSA × DAMASCENA) IN TURKEY VIEW OF MORPHOLOGYCAL AND ANATOMICAL PROPERTIES

[1] Kendir, G., [2] Koroglu, A.

[1]Istinye University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Istanbul, Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

INTRODUCTION:

Rosa × damascena Herrm. (Rosaceae) is one of the most important ornamental plant, cultivated due to its high value aromatic oil, which is used especially in perfumery and pharmaceutical industries (1, 2). Since ancient times, the plant has been used as astringent, analgesic, cardiac and intestinal tonic in folk medicine (1). Turkey is one of the most important rose oil which is known as "Turkish oil rose" and rose concrete producers in the world. It is cultured in especially Isparta, Burdur, Afyon and Denizli, is known as "gül" (2, 3). The aim of this study was to determine whether the samples in different cities of Turkey sold with the name of "gül" carry appropriate qualities for the definition of herbal drug.

MATERIALS AND METHODS:

Rose samples were purchased from different cities of Turkey. Morphological characteristics of all samples were investigated and their purities were checked. The standard sample was obtained from Isparta. The flower materials preserved in 70% alcohol. The cross and surface sections from the sepals and petals were investigated with Sartur reagent (4) under the light microscope. The pollen grains also were surveyed. Furthermore, the characteristic anatomical structures of the powdered samples (standard sample and purchased samples) were determined.

RESULTS:

It was observed that the samples sold were usually composed of rose buds. In the markets, the drug has been sold as an aromatic agent and for the upper respiratory tract. In anatomical examinations, unicellular trichomes were densely observed in the sepal. Druses were determined on the inner surface of sepal. Stomata were present on the outer surface of sepal. Conical papillae with epidermal cells were seen on the petal.

CONCLUSIONS:

The samples do not carry the proper conditions or qualifications for herbal drug description.

REFERENCES:

1. Nayebi N, Khalili N, Kamalinejad M, Emtiazy M (2017). Complementary Therapies in Medicine, 34: 129-140.
2. Ormeci Kart M, Ikiz M, Demircan V (2012). Süleyman Demirel Üniversitesi Ziraat Fakültesi Dergisi, 7: 124-134.
3. Baydar H (2006). Euro Cosmetics, 14: 13-17.
4. Celebioglu S, Baytop T (1949). Farmakognozi Enstitüsü Yayınları, No. 10. Farmakolog 19: 301.

P-003: INVESTIGATION OF MORPHOLOGICAL AND MICROMORPHOLOGICAL FEATURES OF HERBAL MATERIALS SOLD UNDER THE NAME OF KİRAZ SAPI

[1] Kendir, G., [2] Koroglu, A.

[1]Istinye University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Istanbul, Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

INTRODUCTION:

Prunus avium (L.) L. (Rosaceae) is a deciduous tree, usually called sweet cherry, and widely cultured due to its fruits (1).Turkey is one of the biggest sweet cherry producers in the world.The fruits are not only consumed fresh but also used to prepare products, for instance, jam, marmalade, syrup and drinks. Its fruits, fruits stalks and leaves are also used for medicinal purposes (2, 3).This plant grows naturally in northern of Turkey and known as “kiraz” (1).The fruits stalks are used as diuretic and strengthening, and also against diarrhea in Turkey (4). The purpose of present study was to evaluate whether the samples sold under the name of kiraz sapı are suitable for the definition of herbal drug.

MATERIALS AND METHODS:

The fruit stalk samples were purchased from different provinces of Turkey. Morphological properties of these samples were examined and their purities were checked. The standard sample of sweet cherry was obtained from Ankara.The petiole samples preserved in 70% alcohol. The cross and surface sections from the petiole were prepared with Sartur reagent, and demonstrated. Besides, the distinctive anatomical structures of the powdered samples (standard sample and purchased samples) were indicated.

RESULTS:

Open or packed samples are sold. Different morphological characteristics were determined in the samples. In the samples, the fruit parts were observed. It was determined that some samples which sold with the name of kiraz sapı were found to be Prunus cerasus fruits stalks.

CONCLUSIONS:

It is not certain whether the herbal materials sold under the name of kiraz sapı in the market are the right drugs. However, purchased materials are not suitable for human health due to organic and inorganic impurities.

REFERENCES:

1. Browicz K (1972). Cerasus Duhamel. In Davis PH (ed). Flora of Turkey and The East Aegean Islands. Vol. 4. Edinburgh University Press, England, pp 18.
2. Islam A (2002).New Zealand Journal of Crop and Horticultural Science, 30:301-302.
3. Kalyoncu IH, Ersoy N, Yılmaz M (2009). African Journal of Biotechnology, 8:2744-2749.
4. Baytop T (1999). Nobel Tıp Kitabevleri, Istanbul.

P-004: INVESTIGATION OF THE SAMPLES WHICH IS SOLD BY FUMARIA OFFICINALIS L. (ŞAHTERE) NAME IN TURKEY’S MARKET

Biyik, B., Koroglu, A.

Ankara University, Department of Pharmaceutical Botany, Ankara, Turkey

INTRODUCTION:

Fumariaceae family is represented by 7 genera and more than 350 species in the world (1). Fumaria officinalis L., known as ‘‘fumitory’’ in English, ‘‘fumus terrae’’ in Latin and ‘‘şahtere’’ in Turkish is a perennial plant that has been used in empirical medicine for centuries, in Asia and Europe (2). According to Ibn-i Sina ‘‘Şahtere’’ has been effected on purge blood purifiers, itch and scabies and liver congestion (3). This plant is used for rheumatism, skin disorders, hypertension in many countries (4). The aerial parts of this plant is known to be used as a diuretic and blood purifying agent in gall bladder disorders in Turkey; İzmir, Aydin (5). F. officinalis contains isoquinolein alkaloids and flavone heterosides (2).

MATERIALS AND METHODS:

The samples which known as şahtere were purchased from different provinces of Turkey [Ankara (5), Sivas (3), Konya (1), Tokat (1), totally 10 samples]. Information about use of these samples was received. The morphological properties and purities of all samples were examined and photographed (Samsung Galaxy Note 5).

RESULTS:

Findings related to use were matched with the sources. As a result of the morphological studies, the presence of other plants parts (especially Calendula officinalis seeds and Papaver sp. fruits) and foreign matter were determined. Insect infested plant materials were also observed.

CONCLUSIONS:

It has been determined that all of the samples presented to the sale are morphologically formed from the correct drug, namely ‘’şahtere’’ herba. In addition, organic and inorganic contaminants of the samples were not considered suitable for human health.

REFERENCES:

1. Stern RK (1961). Revision of dicentra (Fumariaceae), Department of Biological Sciences, vol. 13, Britonia, p 157.
2. Rabesiaka RL, Havet LJ, Porte C, Fauduet, H (2007). Separation and Purification Technology 54 p 253–261.
3. Sina I (2012). El-Kânun Fi’t-Tıbb II. Kitap. Atatürk Kültür, Dil ve Tarih Yüksek Kurumu, Atatürk Kültür Merkezi Yayını: 378. Çeviren: Esin Kâhya pp 562-563.
4. Sturm S, Strasser ME, Stuppner H (2006). Journal of Chromatography A, 1112 p 331-338.
5. Sari AO, Oguz B, Bilgic A, Tort N, Guvensen A, Senol SG (2010). Anadolu Journal of AARI, 20: p 1-21.

P-005: ANTIOXIDANT AND ANTI-INFLAMMATORY ACTIVITY OF THE FRUITS, STEMS AND LEAVES OF SAMBUCUS EBULUS L.

[1] Cumhur, B., [2] Yilmaz Sarialtin, S., [1] Gumusok S., [2] Coban T., [1] Kilic C.S.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Ankara, Turkey

INTRODUCTION:

Sambucus ebulus L. (Adoxaceae)(dwarf elder) is a widespread annual herbaceous plant which is known as ‘cüce mürver’ in Anatolia (1).This plant is used for common cold, inflammation, rheumatism, burns and infectious wounds cancer treatment traditionally in Turkey, and also has diuretic, expectorant and diaphoretic activities (2).The aim of this study is to investigate the antioxidant activity by using *in vitro* ABTS and DPPH free radical scavenging assays and *in vitro* anti-inflammatory activity by using human red blood cell membrane stabilization assay of *Sambucus ebulus* extracts.

MATERIALS AND METHODS:

Methanol extracts were prepared from the fruits, stems and leaves of the species and evaluated for their free-radical scavenging capacities and antioxidant activities using a number of chemical assays; DPPH and ABTS (2, 3). Human red blood cell membrane stabilization effects of the extracts were evaluated as a mechanism of their anti-inflammatory activities (4).

RESULTS:

ABTS and DPPH free radical scavenging activities were higher for stems than leaves and fruits. Similar to these results, stems showed the strongest anti-inflammatory activity with IC50 values of 1.08 mg/ml, followed by leaf and fruit, respectively (2.4 mg/ml and 6.34 mg/ml).

CONCLUSIONS:

Our results suggest that S. ebulus can be used as a source of natural antioxidants and anti-inflammatory components.

REFERENCES:

1. Atay Balkan I, Ilter Akülke AZ, Bagatur Y, Telci D, Goren AC, Kirmizibekmez H, Yesilada E (2017). Journal of Ethnopharmacology, 206:347-352.
2. Meric ZI, Bitis L, Birteksoz Tan S, Ozbas Turan S, Akbuga J (2014). Marmara Pharmaceutical Journal, 18:22-25
3. Blois MS (1958). Nature, 181:1199–1200.
4. Re R, Pellegrini N, Proteggente A, Pannala A, Yang M, Rice Evans C (1999). Free Radical Biology and Medicine, 26:1231-1237.

P-006: ANTICANCER EFFECT OF EXTRACTS AND ISOLATED COMPOUNDS FROM THE ROOTS OF FERULAGO BLANCHEANA POST EX BOİSS. (APIACEAE) ON CANCER CELL PROLIFERATION

[1] Karakaya, S., [2] Bakar, F., [3] Kilic, C.S., [4] Duman, H.

[1]Atatürk University, Department of Pharmacognosy, Erzurum, Turkey

[2]Ankara University,Department of Biochemistry, Ankara, Turkey

[3]Ankara University,Department of Pharmaceutical Botany, Ankara, Turkey

4Gazi University, Department of Biology, Ankara, Turkey

INTRODUCTION:

Ferulago species have been utilized since ancient times as aphrodisiac, antihelmentic, tonic, carminative, digestive and sedative (1). Apart from its medicinal uses, they have been used as salad or spice by virtue of their special odors. However recent studies report that some Ferulago species have anticancer activity, as well (2). This study reports the in vitro anticancer activity of the aqueous, ethanol extracts and bioactive compounds isolated from the roots obtained from F. blancheana wereinvestigated on MCF-7 human breast and PC3 human prostate cancer cells proliferation.

MATERIALS AND METHODS:

The structures of isolated compounds from the roots of F. blancheana were elucidated by detailed analyses of 1D and 2D NMR and ESI-MS data. Human breast adeno carcinoma cells (MCF-7) and human prostate (PC-3) cells were utilized and measurements were performed via MTT test.

RESULTS:

Five known coumarins such as osthol (1), prantschimgin (2), xanthotoxin (3), felamidin (4), umbelliferone (5) and a knownflavonoid such as rutin (6) were isolated from the roots of F. blancheana. Ethanolic extract of roots from F. blancheana and prantschimgin showed significant anticancer activity on MCF-7 cells with 0.625 and 0.472 mg/mL IC50 values, respectively. On theotherhand, aqueousextract of rootsfrom F. blancheana and umbelliferone showed significant anticancer activity on PC-3 cells with 1.219 and 1.689 mg/mL IC50values, respectively.

CONCLUSIONS:

This study aims to give first report on isolation and characterization of the bioactive compounds from root extracts of F. blancheana and to report anticancer activity on MCF-7 and PC-3 cells of this species.

ACKNOWLEDGEMENTS:

This study was supported by The Scientificand Technological Research Council of Turkey (TUBITAK 115S009).

REFERENCES:

1. Demetzos C, Perdetzoglou D, Gazouli M, Tan K, Economakis C (2000). PlantaMedica 66:560-563.
2. Erdurak CS (2003). In: Investigations on Ferulago isaurica Peşmen and F. syriaca Boiss. (Umbelliferae) species. Ankara University Doctorate Thesis, Ankara.

P-007: ANTICANCER EFFECT OF EXTRACTS AND ISOLATED COMPOUNDS FROM THE ROOTS OF FERULAGO PACHYLOBA (FENZL) BOISS., (APIACEAE) ON CANCER CELL PROLIFERATION

[1] Karakaya, S., [2] Bakar, F., [3] Kilic, C.S., [4] Duman, H.

[1]Atatürk University, Department of Pharmacognosy, Erzurum, Turkey

[2]Ankara University, Department of Biochemistry, Ankara, Turkey

[3]Ankara University, Department of Pharmaceutical Botany, Ankara, Turkey

4Gazi University, Department of Biology, Ankara, Turkey

INTRODUCTION:

Cancer is still a major public health problem in many parts of the world although remarkable progress in decreasing cancer incidence and the developments in chemotherapeutic strategies (1). Ferulago species have been utilized since ancient times as aphrodisiac, antihelmentic, tonic, carminative, digestive and sedative (2). Apart from its medicinal uses, they have been used as salad or spice by virtue of their special odors (3). This study reports the in vitro anticancer activity of the aqueous, ethanol extracts and bioactive compounds isolated from the roots obtained from F. pachyloba were investigated on MCF-7 human breast and PC3 human prostate cancer cells proliferation.

MATERIALS AND METHODS:

The structures of the compounds were elucidated by detailed analyses of 1D and 2D NMR and ESI-MS data. Human breast adenocarcinoma cells (MCF-7) and human prostate (PC-3) cells were utilized and measurements were performed via MTT test.

RESULTS:

Five known coumarins such as osthol (1), prantschimgin (2), xanthotoxin (3), felamidin (4), umbelliferone (5) and a known flavonoid such as rutin (6) were isolated from the roots of F. pachyloba. Ethanolic extract of roots and prantschimgin showed significant activity on MCF-7 cells with 0.559 and 0.472 mg/mL IC50 values, respectively. Also, ethanolic extract of roots and umbelliferone showed significant activity on PC-3 cells with 1.038 and 1.689 mg/mL IC50values, respectively.

CONCLUSIONS:

This study aims to give first report on isolation and characterization of the bioactive compounds from root extracts of F. pachyloba and to report anticancer activity on MCF-7 and PC-3 cells of this species.

ACKNOWLEDGEMENTS:

This study was supported byThe Scientific and Technological Research Council of Turkey (TUBITAK 115S009).

REFERENCES:

1. David AR, Zimmerman MR (2007). Nature Reviews Cancer, 10(10): 728-733.
2. Demetzos C, Perdetzoglou D, Gazouli M, Tan K, Economakis C. (2000). Planta Medica, 66: 560-563.
3. Erdurak CS (2003). In: Investigations on Ferulago isaurica Peşmen and F. syriaca Boiss. (Umbelliferae) species. Ankara University DoctorateThesis, Ankara.

P-008: DETERMINATION OF ANTIOXIDANT AND ANTI-INFLAMMATORY ACTIVITIES OF WALNUT LEAVES (JUGLANS REGIA L.)

[1] Cicek Polat, D., [2] Yilmaz Sarialtin, S., [2] Coban, T., [1] Coskun, M.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Ankara, Turkey

INTRODUCTION:

Walnut tree (Juglans regia L.) can grow naturally in every region of Turkey (1). Walnut leaf is a widely used folk medicine. It has vascular strengthening, anthelmintic, antidiarrheal, antifungal, hypoglycemic, hypotensive and sedative properties. It is used externally as an antiseptic for skin diseases (1, 2). The phytochemicals it contains provide a protective effect against degenerative diseases by reducing oxidative stress and inhibiting macromolecular oxidation (3, 4). In this study, antioxidant and anti-inflammatory activities of walnut leaves were determined.

MATERIALS AND METHODS:

Walnut leaves samples were collected from Savaştepe, Balıkesir. Samples were powdered and extracted with methanol. DPPH• and ABTS•+ free radical scavenging capacity of extract were evaluated for antioxidant activity. The membrane stabilizing activity of the extract was evaluated by using heat-induced human erythrocyte hemolysis as an indicator of anti-inflammatory activity.

RESULTS:

The results of antioxidant and anti-inflammatory activity of Walnut leaves are given in the table.

Antioxidant activity		Extract IC50 ±SD (mg/ml)	BHT IC50 ±SD (mg/ml)
	DPPH• scavenging activities	0,053* ± 0,0015	0,0188*± 0,003
		Extract IC50 ±SD (mg/ml)	Trolox IC50 ±SD (mg/ml)
	ABTS•+ scavenging activities	0,0421* ± 0,0002	0,0151*± 0,008
Anti-inflammatory activity		Extract IC50 ±SD (mg/ml)	Acetylsalicylic acid IC50 ±SD (mg/ml)
	HRBC membrane protection effect	0,3959*± 0,0135	0,2910*±0,08

(*) Statistically significant as compared to control, $p<0.05$ (one-way ANOVA, SPSS 20.0)

CONCLUSIONS:

In conclusion, this study showed that walnut leaves which were collected from Savaştepe (Balıkesir) have significant antioxidant and anti-inflammatory activities. The results we found were similar to other studies (3-5).

REFERENCES:

1. Yigit D, Yigit N, Aktas E, Ozgen U (2009). Türk Mikrobiyoloji Cemiyeti Dergisi, 39:7-11.
2. Baldemir A, Guvenc A (2007). Ankara Eczacılık Fakültesi Dergisi, 36:105-121.
3. Pereira JA, Oliveira I, Sousa A, Ferreira I, Bento A, Estevinho L (2008). Food and Chemical Toxicology, 46:2103-2111.
4. Oliveira I, Sousa A, Ferreira I, Bento A, Estevinho L, Pereira JA (2008). Food and Chemical Toxicology, 46:2326-2331.
5. Chaieb K. Kouidhi B, Slama RB, Fdhila K, Zmantar T, Bakhrouf A (2013). Journal of Herbs, Spices & Medicinal Plants, 19:168-179.

P-009: ANTIOXIDANT POTENTIAL AND ANTI-INFLAMMATORY ACTIVITY OF OLIVE LEAF (OLEA EUROPAEA L.)

[1] Cicek Polat, D., [2] Yilmaz Sarialtin, S., [2] Coban, T.,[1] Coskun, M.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Ankara, Turkey

INTRODUCTION:

Olive leaf (Olea europaea L.) has been used in folk medicine for several thousand of years within Mediterranean countries (1). Olive leaf extract contains many different compounds, which are thought to give the extract its varied therapeutic properties (1,2). Many studies have shown that

olive leaf extract had antiarrhythmic, spasmolytic, immunostimulatory, cardioprotective, hypotensive, anti-inflammatory, antioxidant and anti-thrombotic (1-3). In this study, antioxidant and anti-inflammatory activities of olive leaf collected from two different regions were examined.

MATERIALS AND METHODS:

Olive leaf samples were collected from Edremit (Balıkesir) and Tirilye (Bursa). Samples were powdered and extracted with methanol. DPPH• and ABTS•+ free radical scavenging capacity of extract were evaluated for antioxidant activity. The membrane stabilizing the activity of the extract was evaluated by using heat-induced human erythrocyte hemolysis as an indicator of anti-inflammatory activity.

RESULTS:

The results of antioxidant and anti-inflammatory activity of Olive leaf extracts are given on the table.

Antioxidant activity	DPPH• scavenging activities	Extract (Edremit)	Extract (Tirilye)	BHT
	IC50 ±SD (mg/ml)	0,4401*±0,0210	0,0579±0,0002	0,0188*±0,003
	ABTS•+ scavenging activities	Extract (Edremit)	Extract (Tirilye)	Trolox
	IC50 ±SD (mg/ml)	0,3597*±0,0245	0,0499*±0,0003	0,0151*±0,008
Anti-inflammatory activity	HRBC membrane protection effect	Extract (Edremit)	Extract (Tirilye)	Acetylsalicylic acid
	IC50 ±SD (mg/ml)	0,4462*±0,0074	0,4769*±0,0104	0,2910*±0,08

(*) Statistically significant as compared to control, $p<0.05$ (one-way ANOVA, SPSS 20.0)

CONCLUSIONS:

In conclusion, this study showed that olive leaf samples which were collected from Tirilye (Bursa) have significant antioxidant and anti-inflammatory activity. The results we found were similar to other studies (2-4).

REFERENCES:

1. Lee OH, Lee BY (2010). Bioresource Technology, 101:3751-3754.
2. Sudjana AN, D'Orazio C, Ryan V, Rasool N, Ng J, Islam N, Riley TV, Hammer KA (2009). International Journal of Antimicrobial Agents, 33:461-463.
3. Benavente-Garcia O, Castillo J, Lorente J., Ortuño A, Rio JAD (2000). Food Chemistry, 68:457-462.
4. Wang L, Geng C, Jiang L, Gong D, Liu D, Yoshimura, Zhong L (2008). European Journal of Nutrition, 47:235-243.

P-010: INVESTIGATION OF THE SAMPLES WHICH IS SOLD AS PASSIFLORA (ÇARKIFELEK) NAME IN MARKET

Kose E.C., Koroglu A.

Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

INTRODUCTION:

Passiflora L. (Passifloraceae) consists herbaceous or woody tendril climber plants, commonly spread in the warm temperate and tropical regions of the World (1). It is especially used for the treatment of insomnia and anxiety (2). This genus is known usually as "çarkıfelek or passiflora" in Turkey. Aim of the study is to investigate suitability of the samples sold in the market from a morphological point of view, for public health.

MATERIALS AND METHODS:

The samples which known as çarkıfelek or passiflora were purchased from the markets in Ankara. It is used as a standard for the identification of the morphological characteristics of the fruit obtained from the culture form of Passiflora incarnata L. The samples were examined morphologically according to the drug character defined in the Turkish Pharmacopoeia and European Pharmacopoeia.

RESULTS:

Despite herba of Passiflora incarnata being used as a drug, it has been determined that there is no sale of drug obtained from this plant in the Ankara market. As a result of the studies, it was determined that two of the samples are fruits of Paliurus spina-christi Mill. It is sold under the name of passiflora or çarkıfelek roots was found to be Caiophora lateritia (Hook.) Benth. (Loasaceae) fruits which does not grow in our country.

CONCLUSIONS:

The products sold under the name of çarkıfelek (passiflora) in Ankara are not the right drugs obtained from the right plant. For this reason, it can not be expected to show the intended effect in terms of health. These products should be inspected before and during sales.

REFERENCES:

1. Patel SS, Soni H, Mishra K, Singhai AK (2011). International Journal of Research in Phytochemistry and Pharmacology, 1:1-16
2. Miroddi M, Kalapai G, Navarra M, Minciullo PL, Gangemi S (2013). Journal of Ethnopharmacology, 150:791-804.
3. European Pharmacopoeia, Council of Europe (2010). 7th ed., Strasbourg: European Directorate for the Quality of Medicines & HealthCare.
4. T.C. Sağlık Bakanlığı Türkiye İlaç ve Tıbbi Cihaz Kurumu (2016). Türk Farmakopesi-II Monograflar, (Avrupa Farmakopesi Adaptasyonu) 1. Baskı. Ankara.

P-011: EXAMINATION OF CAPSELLA BURSA-PASTORIS L. SPECIMENS SOLD IN THE MARKET IN TERMS OF MORPHOLOGICAL CHARACTERISTICS AND MICROBIOLOGICAL CONTAMINATION

[1] Koroglu A., [1] Kose E.C., [2] Simsek, D., [2] Altanlar, N.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Ankara, Turkey

INTRODUCTION:

Capsella bursa-pastoris (L.) Medik. is an annual or biennial herb (Brassicaceae). Diverse groups of biological activities are reported to be present in the different plant parts of C. bursa-pastoris which possessed, anti-inflammatory, antioxidant, antimicrobial, and antihypertensive activities. It is usually used for liver and kidney inflammation (1). This genus is known usually as 'çoban çantası' in Turkey. Aim of the study is to evaluate the suitability of the samples sold in the market for public health in terms of microbiological contamination.

MATERIALS AND METHODS:

Seven different samples known as 'çoban çantası' were purchased from the markets in Ankara. Morphological studies were carried out on the standard sample (AEF 27190) and purchased market samples. These 7 different samples purchased were examined for microbiological contamination. Microbial contamination studies were done by plate counting method. The presence of contamination in the samples was determined according to the European Pharmacopoeia (2011) (2).

RESULTS:

As a result of the microbiological studies, pathogen microorganism are not shown to be present in any samples, however number of microorganisms have been found to be higher than the limits provided in the European Pharmacopoeia. As a result of the morphological study, foreign matter and foreign plants were encountered.

CONCLUSIONS:

Usage of samples in the market for treatment is inconvenient because samples are not suitable for the number of bacteria and molds according to the European Pharmacopoeia. According to our findings, it is not appropriate to use these specimens sold on the market as a therapeutic.

REFERENCES:

1. Ma Q, Guo Y, Wei R, Sang Z, Liu W, Gao L, Liu T (2016). Revista Brasileira de Farmacognosia, 26:710-713.
2. European Pharmacopoeia 7.0.5.1.4. Microbiological quality of non-sterile for pharmaceutical use. Strasburg, 2011.

P-012: TOTAL PHENOLIC CONTENT AND ANTIOXIDANT CAPACITY OF SOME SELECTED TURKISH ECHINOPHORA L. SPECIES

[1] Yuzbasıoglu Baran, M., [2] Zare, G., [3] Dogru Koca, A., [1] Kuruuzum Uz, A.

[1]Hacettepe University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

[2]Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

[3]Hacettepe University, Faculty of Science, Department of Biology, Ankara, Turkey

INTRODUCTION:

The genus Echinophora L. (Apiaceae) with eleven species in the world is represented by six species in the flora of Turkey which three of them are endemics (1). The aerial parts of some species are used in folk medicine to wound-healing properties and to treat gastric ulcers. E. tenuifolia subsp. sihthorpiana known as "Çörtük, Cördük and Tarhana Otu" in Turkey also used as spice for food (2, 3). In this study total phenolic contents and antioxidant capacity of these taxa contain: E. orientalis Hedge & Lamond, E. tenuifolia subsp. sihthorpiana (Guss.) Tutin, E. tournefortii Jaub. & Spach and E. lamondiana Yildiz & Z.Bahcecioglu (endemic) have been studied.

MATERIALS AND METHODS:

Antioxidant capacity of the Echinophora MEOH extracts were determined by DPPH radical scavenging and ABTS total antioxidant capacity assays (5).

RESULTS:

Results of the DPPH assay showed E. tournefortii (IC50=61.72 µg/mL), E. lamondiana (IC50= 108.10 µg/mL) E. orientalis (IC50=123.90 µg/mL), E. tenuifolia subsp. sihthorpiana,(IC50=193.50 µg/ml) showed low and moderate radical scavenging activity. ABTS+ total antioxidant capacities of the extracts found as 229.74mg/g, 69.6mg/g, 194.15mg/g and 166.2mg/g trolox equivalent, respectively.

CONCLUSIONS:

The results showed that all MeOH extracts possessed antioxidant properties including DPPH radical scavenging and ABTS antioxidant capacity assays. Total phenolic content will be determined for each extract. Our antioxidant activity studies are continuing and isolation studies will be carried on the most active extract.

ACKNOWLEDGEMENTS:

In this study field works were supported by a grant of TUBITAK (216Z034).

REFERENCES:

1. Güner A, Aslan S, Ekim T, Vural M, Babac, MT (Eds.) (2012). Türkiye Bitkileri Listesi (Damarlı

Bitkiler). Istanbul: Nezahat Gökyiğit Botanik Bahçesi ve Flora Araştırmaları Derneği Yayını.
2. Baytop T (1984). Türkiyede bitkiler ile tedavi. Istanbul University Press, Istanbul, p 40.
3. Degirmencioglu N, Gocmen D, Dagdelen A, Dagdelen F (2005). Food Technology and Biotechnology, 43: 175-179.
4. Genc I, Ecevit Genc G (2014). Istanbul Eczacilik Fakültesi Dergisi, 44: 233-240.
5. Zhang Q, Zhang J, Shen J et al. (2006). Journal of Applied Phycology, 18: 445–450.

P-013: COMPARATIVE STUDY OF ANTICANCER ACTIVITIES OF FOUR ALLIUM L. SPECIES EXTRACTS AGAINST MCF-7 CELLS

[1] Eksi Bona, G. [2] Akalin Ciftci, G. [1] Gencler Ozkan, A.M.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

[2]Anadolu University, Faculty of Pharmacy, Department of Biochemistry, Eskisehir, Turkey

INTRODUCTION:

Allium L. species are the one of the oldest plants cultivated for its utilization as food and medicine. It has numerous useful impacts such as antithrombotic, antimicrobial, antiarthritic, antitumor, hypoglycemic activities (1, 2). Various studies have showed chemopreventive action of the organosulfur compounds and anticancer activity has been ascribed to organosulfur compounds in Allium species. This also leads to its impact on inhibition of tumor growth (3). In this study, four Allium species (A. callidyction, A. peroninianum, A. hirtovaginatum and A. callimischon subsp. haemostictum) have been investigated and their anticancer activities are compared (4).

MATERIALS AND METHODS:

Plants were collected from Muğla, Kahramanmaraş and İstanbul provinces in Turkey. Ethanol extracts were prepared from the plant and cytotoxicity tests of the extracts were performed. In vitro cytotoxic effects of the extracts were determined by MTT assay using MCF-7 (human breast cancer) cell lines.

RESULTS:

Cytotoxic effect was found to be high in ethanolic extracts. In the DNA synthesis inhibition tests, the extracts were found to show high inhibition compared to the cisplatin used as control. Extracts have shown to have significant cytotoxic effect on MCF–7 cell lines.

CONCLUSIONS:

While the extract of A. callimischon subsp. haemostictum has showed to have best early apoptotic effect, the extract of A. callidyction has showed the best late apoptotic effect. Thus, the examined Allium species can be promising agents in respect to their anticancer effects.

ACKNOWLEDGEMENTS:

This study was supported by a grant of BAP (16H0237012).

REFERENCES:

1. Block E (2010). Garlic and Other Alliums: The Lore and the Science. RSC Publisher.
2. Friesen N, Fritsch RM, Blattner FR (2006). Aliso, 22: 372–395.
3. Jun Z, Suzuki M, Xiao J, Wen J, Talbot SG, Li GC, Xu M (2009). Biotechnol Appl Biochem, 52: 113-119.
4. Kollmann F (1984). In: David PH (ed). Allium L. In: Flora of Turkey and the East Aegean Islands. Edinburgh Univ. Press. pp 98–211.

P-014: ANATOMICAL STUDY ON CORDIA MYXA L. (BORAGINACEAE) LEAF

[1] Kendir, G., [2] Koroglu, A.

[1]Istinye University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Istanbul, Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

INTRODUCTION:

Cordia L. (Boraginaceae) is represented by one species (Cordia myxa L.) in Turkey. It is estimated that Cordia myxa originates from the eastern Mediterranean region of eastern India. It is a deciduous tree, known as “Yellim ağacı” and grows only in Hatay province of Turkey. The plant is cultured for various purposes, and has edible fruits (1-3). Decoction of the leaves has been used against cough and cold in India (4). The objective of this study is to investigate anatomical properties of the Cordia myxa leaves growing in Turkey.

MATERIALS AND METHODS:

The plant materials were collected from Hatay. The leaf materials stored in 70% alcohol. The cross and surface sections of the leaves were examined with Sartur reagent (5) under the microscope and, the images on the light microscope were taken with a Leica DM 4000 B camera.

THE RESULTS:

The leaf is hypostomatic and bifacial. In palisade parenchyma, cystoliths cells were determined. Many unicellular trichomes with cuticle striated were observed. The trichomes with cystolith also were seen. Glandular hairs composed of a one or two-celled stalk and a unicellular head are present in the lower epidermis. Crystals include formations in different shapes such as prismatic and crystal sand. The stomata are anomocytic type (3-6 subsidiary cells).

CONCLUSIONS:

Anatomical structure of Cordia myxa leaves growing in Turkey was demonstrated for the first time.

REFERENCES:

1. Edmondson JR (1978). Cordia L. In Davis PH (ed). Flora of Turkey and The East Aegean Islands. Vol. 6. Edinburgh University Press, Edinburgh, pp 246.
2. Guner A, Aslan S, Ekim T, Vural M, Babac MT (eds) (2012). Türkiye Bitkileri Listesi (Damarlı Bitkiler). Nezahat Gökyiğit Botanik Bahçesi ve Flora Araştırma Derneği Yayını, Istanbul.
3. Meghwal PR, Singh A, Morwal BR (2014). Genetic Resources and Crop Evolution, 61:1633-1643.
4. Rao PK, Hasan SS, Bhellum BL, Manhas RK (2015). Journal of Ethnopharmacology, 171:12-27.
5. Celebioglu S, Baytop T (1949). Farmakognozi Enstitüsü Yayınları, No:10. Farmakolog, 19:301.

P-015: COMPARATIVE FRUIT ANATOMY AND MORPHOLOGY OF SOME SPECIES KNOWN AS CUMIN (KIMYON) WHICH IS USED TRADITIONALLY IN TURKEY

Tuncay, H.O., Yesil, Y.

Istanbul University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Istanbul, Turkey

INTRODUCTION:

Herbs and spices have long been used to improve the flavour of food. Cumin, one of these spices, is widely used all over the world. However different species known as Cumin are used for the same purpose (1, 2). According to the data obtained from ethnobotanical studies in Turkey, four species are known and used as Cumin (Kimyon) in Turkey; Carum carvi, Cuminum cyminum, Laser trilobum and Grammosciadium daucoides. In this study, comparative fruit anatomy and morphology of these species were studied (3, 4).

MATERIALS AND METHODS:

Anatomical research material was dried, so first of all they were kept in distilled water, then they were preserved in 70% ethanol. In this study at least 6 mature fruits of each of 4 species were studied. All transverse sections were cut by hand from the middle of the mericarps using a blade. Samples were examined in Sartur reagent (5).

RESULTS:

Considerable differences were observed in the fruit morphology of these species having different fruit shapes. Also, the fruit surface patterns of species show important differences, the only similarity related to their surfaces was being striated. However, Carum carvi and Grammosciadium daucoides have prominent striae, Cuminum cyminum and Laser trilobum have slight striae. Fruits have anatomical shapes and extent of costal channels and the presence of secondary and primary ribs are important differences. An identification key based on both morphological and anatomical characters is presented for the studied species.

CONCLUSIONS:

The anatomical and morphological results will allow separation of the species known as cumin.

ACKNOWLEDGEMENTS:

This work was supported by Scientific Research Projects Coordination Unit of Istanbul University, Project number: 25239.

REFERENCES:

1. Tuzlacı E (2011). Alfa Basım Yayım Dağıtım San. ve Tic. Ltd. Şti. Istanbul.
2. Chevallier A (2016). Encyclopedia of Herbal Medicine: 550 Herbs and Remedies for Common Ailments, Third ed. Dorling Kindersley Book, USA, pp 197.
3. Menemen Y, In: Güner A, Aslan S, Ekim T, Vural M, Babaç MT (eds) (2012). Türkiye Bitkileri Listesi/Damarlı Bitkiler. Nezahat Gökyiğit Botanik Bahçesi ve Flora Araştırmaları Derneği Yayını. Istanbul, Turkey.
4. Hedge IC, Lamond JM (1972). In: Davis, P. H. (ed.), Flora of Turkey and the East Aegean Islands, (4) Edinburgh University Press, Edinburgh.
5. Baytop T (1984). Therapy with medicinal plants in Turkey (Past and Present), Publications of the Istanbul University, No. 3255, Istanbul.

P-016: ENDEMISM IN ISTANBUL PLANTS

Tuncay, H.O., Akalın, E.

Istanbul University, Department of Pharmaceutical Botany, Istanbul, Turkey

INTRODUCTION:

Istanbul has an extraordinary plant variety due to its diversity of soil, geographical position between two seas and two continents, climate, topography and traditional land use. Istanbul is also home to many endemic plants in the same way. At the same time these plants are threatened by intensive urbanization in recent years (1).

MATERIALS AND METHODS:

Firstly, a list of endemic plants from İstanbul was created according to “Flora of Turkey and the East Aegean Islands”, articles and books (2). Previously created lists were also checked (3, 4). Herbarium records of the plants in this list have been checked. The plants collected from outside Istanbul were

identified and only a list of plants growing in Istanbul was established. Literature records of the plants were checked (5).

RESULTS:

With this study, endemic plants growing in Istanbul were detected. 60 plants endemic to Turkey are growing up in Istanbul. Only 10 of these plants are endemic to Istanbul. 25 of these plants are found in Istanbul and its surrounding areas (neighboring cities). The remaining 25 plants are more common endemics and also are found in Anatolia.

CONCLUSIONS:

This study shows that among 60 of Turkey's endemic plants that are found in Istanbul only 10 of them are endemic to Istanbul. It is very important to follow up these plants immediately and protect them from harmful effects of urbanization.

ACKNOWLEDGEMENTS:

We would like to thank to Prof. Dr. Neriman Özhatay for her contributions. Thanks to Dr. Sırrı Yüzbaşıoğlu and Tamer Avcı for providing plant photos.

REFERENCES:

1. Ozhatay N, Kocyigit M, Bona M (2012). Türkmenler Matbaacılık Rek. San. Tic. Ltd.Şti, Istanbul.
2. Davis PH. (ed.) (1965-1988), Flora of Turkey and the East Aegean Islands, vol.1-10. University Press, Edinburgh.
3. Ozhatay N, Ozhatay E, Erdem AO (2010). Şile'nin Doğal Bitkileri, Işık Üniversitesi Yayınları-02, Istanbul.
4. Akkemik U (2016). İstanbul'un Doğal Bitkileri. Cinius Yayınları, Istanbul.
5. Güner A, Aslan S, Ekim T, Vural M, Babaç MT (Eds) (2012). 'Türkiye Bitkileri Listesi/Damarlı Bitkiler'. Nezahat Gökyiğit Botanik Bahçesi ve Flora Araştırmaları Derneği Yayını, Istanbul.

P-017: HPTLC EXAMINATION OF VARIOUS KEDIOTU (VALERIAN; VALERIANA OFFICINALIS L.) SAMPLES SOLD IN THE MARKET OF TURKEY

[1] Gumusok, S., [2] Gokbulut, A., [1] Koroglu, A.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

"Kediotu" (Valeriana officinalis L.) samples were investigated and findings were compared with the monographs found in European Pharmacopoeia 2011 and Turkish Pharmacopoeia II, as well as chemical profile of the samples were examined (1-3).

MATERIALS AND METHODS:

20 different samples of kediotu were purchased from local markets in different cities of Turkey. Morphological structure of the kediotu samples was determined. The chemical profile of the investigated samples was compared with the valerianic acid (=standard sample) by using a HPTLC method.

RESULTS:

Kediotu samples were determined that the majority of the samples purchased from the market consisted of leaves or parts of herbs, which were not identified as root samples. This finding was especially striking for the 10 different samples which were purchased from the capital city markets. Among the 10 samples sold under the name of kediotu, only two of them belong to the root, and the other 8 samples consist of leaf and aerial parts of the different plants. Moreover, in parallel to the morphological study results, chemical composition of the samples was not found to be identical with the standard sample. Chemical profile of most of the samples was different from each other according to the HPTLC results.

CONCLUSIONS:

It has been observed that the investigated kediotu samples which are offered for sale in the market of Turkey do not confirm to the definition of scientific drug in terms of morphological characteristics and chemical content. Most of the investigated samples which are not supposed to be kediotu, are possibly contaminated with organic and inorganic substances so that they should not be used for public health.

REFERENCES:

1. Gumusok S, Koroglu A (2016). Kediotu (Valeriana officinalis L.) adı ile piyasada drog olarak satılan örnekler üzerinde morfolojik çalışmalar, BİHAT 22nd, Book of Abstract, pp 152.
2. Council of Europe, European Pharmacopeia (2011). Council of Europe Press. 7th Edition, p 1261.

3. T.C. Sağlık Bakanlığı Türkiye İlaç ve Tıbbi Cihaz Kurumu (2016). Türk Farmakopesi-II Monograflar (Avrupa Farmakopesi Adaptasyonu), Ed. Anıl Reklam Matbaa Ltd. Şti, p 1563, Ankara.

P-018: DETERMINATION OF ANTI-INFLAMMATORY AND ANTI-ANTIOXIDANT ACTIVITIES OF OPOPANAX HISPIDUS

[1] Gumusok, S., [2] Yilmaz Sarialtin, S., [2] Coban, T., [1] Kilic, C.S.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Ankara, Turkey

INTRODUCTION:

Opopanax W. Koch (Apiaceae) species, belonging to Apiaceae family are known with the names Kaymakotu in our country and known as Hercules' all-heal throughout the world. English name of the species gives us a hint on the medicinal usage of them. In respect to etymology "opos" means vegetable juice and "panax" (panacea) means all-healing, universal remedy. Traditional use of Opopanax ssp. are expectorant and antispasmodic (1). This study was designed to assess the *in vitro* antioxidant activity, anti-inflammatoryactivity and free radical scavenging capacity of O.hispidus.

MATERIALS AND METHODS:

Methanol extracts were prepared and evaluated for their free-radical scavenging capacity and antioxidant activity using a number of chemical assays; DPPH and ABTS (2, 3). Human red blood cell membrane stabilization effects of extracts were evaluated as a mechanism of the anti-inflammatory activity (4).

RESULTS:

The DPPH and ABTS radical scavenging activities were higher for herbs than flowers. Flowers were found to be more effective in anti-inflammatory assay than herbs with IC50 values of 3.31 mg/ml and 4.75 mg/ml, respectively.

CONCLUSIONS:

Phenolic substances are known to be responsible from the antioxidant effect that medicinal plants possess. Flowers and especially yellow flowers are known to be rich in flavonoids, therefore it is not surprising that flowers were found to be more effective than aerial parts and further studies have to be performed to determine the flavonoid and total phenolic content of this species (5).

REFERENCES:

1. Muckensturm B, Boulanger A, Ouahabi S, Reduron JP (2005). Fitoterapia, 76: 768–770.
2. Blois MS (1958). Nature, 181:1199–1200.
3. Re R, Pellegrini N, Proteggente A, Pannala A, Yang M, Rice-Evans C (1999). Free Radical Biology & Medicine, 26:1231-1237.
4. Debnath PC, Das A, Sajib AI, Hassan MM (2013). Pharmacognosy Journal, 5:104-107.
5. Samuelsson G, Bohlin L. (Eds.) (2009). Drugs of Natural Origin-A Treatise of Pharmacognosy, Swedish Pharnaceutical Society, Sweden.

P-020: THE ANTITYROSINASE ACTIVITY OF ARBUTUS UNEDO L. LEAVES

[1] Koyu, H., [2] Demir, S., [2] Baykan, S.

[1]Izmir Katip Celebi University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Izmir, Turkey

[2]Ege University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Izmir, Turkey

INTRODUCTION:

Arbutus unedo L. (Koca yemiş) is an evergreen shrub in the family Ericaceae and widespread in the Mediterranean regions. Different parts of this plant have long been used in folk medicine against several diseases, mainly gastrointestinal and urological problems (1). Tyrosinase is a well-known key enzyme in melanin biosynthesis in skin, hair and has also been proposed to contribute to the formation of neuromelanin. In cell culture systems, expression of tyrosinase increases neuronal susceptibility to oxidizing conditions, including dopamine itself which is related to Parkinson disease (2). Tyrosinase inhibitors have become increasingly important because of their potential use as hypopigmenting agents. Antityrosinase activity of A. andrachne was previously reported (3). In this study antityrosinase activity of A. unedo leaves was evaluated.

MATERIALS AND METHODS:

Air dried A. unedo leaves were extracted with dichloromethane and ethanol separately. Extracts were fractionated with RP-C18 and antityrosinase activity of fractions were investigated with an assay that 96-well microplate was adopted and optimized for tyrosinase inhibitory activity from a previously described method using kojic acid as reference drug (4).

RESULTS:

EtOH fractions (water:MeOH 50:50, 75:25 and 25:75 elutes) were found as mainly responsible for tyrosinase inhibitory activity at 1.25 mg/ml concentration and the % inhibition values were 89.14, 81.22 and 58.01 respectively.

CONCLUSIONS:

The fractionation process with water and methanol demonstrated that A. unedo leaves hold a potential for tyrosinase inhibitory activity. Active fractions proved

to be promising for future research as a natural alternative for inhibition of tyrosinase activity and further phytochemical studies for active secondary metabolites are scheduled.

REFERENCES:

1. Oliveira, I, Baptista, P, Bento, A, Pereira, JA (2011). Journal of Food and Nutrition Research, 50(2):73-85.
2. Greggio E, Bergantino E, Carter D, Ahmad R, Costin GE, Hearing VJ et al. (2005). Journal of Neurochemistry, 93(1):246-56.
3. Issa R, Afifi F, Amro B. International Journal of Cosmetic Science, 30(4):271-6.
4. Koyu H, Kazan A, Demir S, Haznedaroglu MZ, Yesil-Celiktas O (2018). Food Chemistry, 248:183-91.

P-021: THE EFFECT OF PRANGOS PABULARIA LINDL. ON ERECTILE DYSFUNCTION ASSOCIATED WITH H2S

[1] Baykan, S., [2] Sevin, G., [2] Alancay, E., [1] Albayrak, G., [2] Yetik, G.

[1]Ege University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Izmir, Turkey

[2]Ege University, Faculty of Pharmacy, Department of Pharmacology, Izmir, Turkey

INTRODUCTION:

Prangos pabularia Lindl. is a perennial herb which is distributed in North, East and Southeast Anatolia and the plant is known as ''Beyik and Caksır'' in Anatolia (1). P. pabularia has been used as aphrodisiac in traditional medicine. However the scientific background of this has not been investigated enough. Thus, we aimed to study i) whether the extract of the root of P. pabularia (10-12-10-4 g/mL) has a relaxant effect ii) the role of H2S; a strong erectile gasotransmitter (2), in the mechanism of this possible relaxation response caused by P. pabularia extract in mice penile tissues.

MATERIALS AND METHODS:

Air dried roots were extracted with hexane, chloroform and methanol sequentially. DMT strip myograph is used to measure relaxation response on chloroform extract.

RESULTS:

P. pabularia caused concentration-dependent relaxation responses (P<0,001, ANOVA, vehicle vs extract). However, propargylglycine (PAG; 30 min., 10mM), an inhibitor of the H2S producing enzyme-cystathionine γ lyase (CSE) did not inhibit these relaxations.

CONCLUSIONS:

This results show that the extract has relaxant effects on penile tissue and H2S formation is not involved in relaxant effects of the extract of P. pabularia.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-117S116)

REFERENCES:

1. Güner A (2012). Türkiye bitkileri listesi:(darmarlı bitkiler): ANG Vakfı.
2. Yetik-Anacak G, Sevin G, Ozzayim O, Dereli MV, Ahmed A (2016). Vasc Pharmacol, 87:76-82.

P-022: MAJOR FURANOCOUMARINS OF PRANGOS PABULARIA LINDL.

Demiroz, T., Demir, S., Baykan, S.

Ege University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Izmir, Turkey

INTRODUCTION:

Prangos sp. (Apiaceae) includes 17 species in flora of Turkey, 9 of which are endemic (1). Roots of the Prangos species, called as “Caksir” are used as aphrodisiac, wound healing and haemostatic in Anatolian traditional medicine (2). Previous phytochemical investigations on roots of Prangos indicate the major compounds as coumarins and furanocoumarins derivatives (3, 4). The aim of this study is to determine the major chemical compounds of Prangos pabularia Lindl.

MATERIALS AND METHODS:

Roots of plant extracted by n-hexane, chloroform and methanol, sequentially. Major compounds in chloroform extract were isolated by different chromatographic techniques and characterized by spectroscopic methods such as 1-D, 2-D NMR and LC-MS. Percentage of relative amounts of three major compounds in extract were determined by HPLC.

RESULTS:

Three major compounds of P. pabularia were identified as oxypeucedanin (9.96%), isoimperatorin (9.26%) and imperatorin (5.2%).

CONCLUSIONS:

Major compounds are well known furanocoumarins and should be responsible for the possible effects of the plant.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-117-S-116)

REFERENCES:

1. Güner A (2012). Türkiye Bitkileri Listesi (Damarlı Bitkiler). Nezahat Gökyiğit Botanik Bahçesi ve Flora Araştırmaları Derneği Yayını, Turkey, pp 75-76

2. Baykan S, Oztürk B, Sahin B, Senol SG (2014). "UNESCO Dünya Kültür Mirasında Yer Alan Nemrut Dağı ve Çevresinin Etnobotanik Yönden Araştırılması" XXI. Bitkisel İlaç Hammaddeleri Toplantısı, Kayseri.
3. Shikishima Y, Takaishi Y, Honda G, Ito M, Takeda Y, Kodzhimatov OK, Ashurmetov O, Lee KH (2001). Chemical and Pharmaceutical Bulletin, 49(7):877-880.
4. Razavi SM, Nazemiyeh H, Delazar A, Hajiboland R, Rahman MM, Gibbons S, Nahar L, Sarker SD (2008). Phytochemistry Letters, 1:159-162.

P-024: EFFECT OF ANTI-BIOFILM AGENTS AND ANTIBIOTICS ALONE AND IN COMBINATIONS AGAINST BIOFILMS OF CATHETER-ASSOCIATED COAGULASE-NEGATIVE STAPHYLOCOCCI

[1] Ozturk, I., [1] Tekintas, Y., [2] Temel, A., [2] Ermertcan, S., [3] Kurutepe, S., [3] Hosgor Limoncu, M.

[1]Izmir Katip Çelebi University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Izmir, Turkey

[2]Ege University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Izmir, Turkey

[3]Celal Bayar University, Faculty of Medicine, Department of Medical Microbiology, Manisa, Turkey

INTRODUCTION:

In this study, the effects of antibiotics and antibiofilm agents alone and in combination were investigated against biofilms of coagulase-negative Staphylococci (CNS) isolates that were isolated from catheters at Celal Bayar University Hospital.

MATERIAL AND METHODS:

Minimum inhibitory concentrations (MIC) of antibiofilm agents (N-acetylcysteine, EDTA, nisin, farnesol) and antibiotics (gentamicin, ciprofloxacin, doxycycline, rifampicin) against 45 isolates were determined by microdilution method according to EUCAST.The combined effects of the agents were investigated by checkerboard method.The biofilm production of isolates were investigated by spectrophotometric microplate method.

RESULTS:

The MIC of N-acetylcysteine was 1024 µg/ml in 33 isolates, MIC of EDTA was 256 µg/ml in 25 isolates, MIC of nisin was 128 µg/ml in 29 isolates and MICs of farnesol was 512 µg/ml in 13 isolates, respectively. The biofilm production capacities and resistance profiles to antibiotics of isolates are shown in Table 1.

Table 1. Biofilm production and resistance profiles to antibiotics of the isolates.

Biofilm production	Number of isolates	Antibiotics	Number of resistant isolates
Non-biofilm	-	Gentamicin	28 (% 62.2)
Weak	6 (% 13.3)	Ciprofloxacin	29 (% 64.4)
Moderate	15 (% 33.3)	Doxycycline	7 (% 15.6)
Strong	24 (% 53.3)	Rifampicin	19 (% 42.2)

Biofilm production was inhibited with the combinations of EDTA+rifampicin in total of nine isolates that produced strong biofilm, with nisin+doxycycline combinations in seven isolates, with nisin+gentamicin combinations. The mature biofilm levels were decreased with the combinations of farnesol+rifampicin in six isolates and with nisin+ciprofloxacin, nisin+doxycycline and nisin+rifampicin combinations in five isolates.

CONCLUSIONS:

The antibiofilm agents alone and in combination with antibiotics could prevent catheter colonization and it is thought that morbidity and health care costs will be positively affected with using of these agents.

P-025: ANTIBIOFILM ACTIVITIES OF SELECTIVE SEROTONIN REUPTAKE INHIBITORS AGAINST CLINICAL CANDIDA ISOLATES

[1] Tekintas, Y., [2] Temel, A., [2] Ates, A., [2] Erac, B., [3] Metin, D.Y., [3] Hilmioglu Polat, S., [2] Hosgor Limoncu, M.

[1]Izmir Katip Celebi University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Izmir, Turkey

[2]Ege University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Izmir, Turkey

[3] Ege University, Faculty of Medicine, Department of Medical Microbiology, Izmir, Turkey

INTRODUCTION:

Candida spp. are opportunistic fungi that often cause hospital infections.. Biofilm formation is an important virulence factor of Candida sp. because its resistance to several antifungal drugs makes it difficult to eradicate.The aim of this study was to determine antibiofilm activity of selective seratonin reuptake inhibitors (SSRIs) sertraline, paroxetine, fluoxetine against different Candida spp.

MATERIALS AND METHODS:

Twenty Candida sp. (C. albicans: 6, C. glabrata: 3, C. krusei: 4, C. tropicalis: 4, C. parapsilosis: 3) isolated from Ege University Hospital and Candida parapsilosis ATCC 22019 strain were examined. The inhibitory concentrations of the SSRIs were evaluated by broth microdilution method according to EUCAST criteria in a previous study (Microbiologica Balkanica 2017/AntM-43). The biofilm production of isolates and

the effects of the SSRI molecules on mature biofilm were determined by spectrophotometric microplate method.

RESULTS:

Seven of the isolates were weak, nine of them were moderate, four isolates were identified as strong biofilm producers. C. parapsilosis showed the highest biofilm production, whereas C. albicans showed the lowest one. The effects of SSRIs on mature biofilm structure in moderate and strong biofilm producer isolates were shown in Table 1.

Table 1. Effects of SSRIs to biofilm production in moderate and strong biofilm producer isolates

		Selective Seratonin Reuptake Inhibitors					
	Effects on Biofilm	FLX (MIC/2)	FLX (MIC/4)	PRX (MIC/2)	PRX (MIC/4)	SRT (MIC/2)	SRT (MIC/4)
Number of isolates	Reduced	6	4	3	-	5	3
	Induced	2	4	7	7	3	3
	Stable	5	5	3	6	5	7

FLX: Fluoxetine, PRX: Paroxetine, SRT: Sertraline, MIC: Minimum Inhibitory Concentrations

CONCLUSIONS:

Biofilm production can vary depending on the species of Candida. Sub-MIC concentrations of SSRI molecules have inducing or reducing effects on different species of Candida sp.

P-026: DETERMINATION OF ACID DISSOCIATION CONSTANT AND ANTI MICROBIAL ACTIVITY OF CONDENSED 1,4-DIHYDROPYRIDINE DERIVATIVES

[1] Gunduz, MG., [2] Ozkul C., [3] Kocak E.

[1]Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

[2]Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Ankara, Turkey

[3]Hacettepe University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Determination of acid dissociaition constant (pKa) that provides the ratio of ionized form concentration and unionized form concentration of a drug molecule inside body is the first stage for drug development. Drug absorption, distribution, metobolism, excretion process are depend on pKa value of molecules (1). To evaluate molecular properties of ethyl (CE2)/ 2-(Methacryloyloxy)ethyl (CE7) 2,6,6-trimethyl-4-(1-naphthyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate derivatives, pka values were calcualted. Moreover, antimicrobial activity was evaluated to understand whether new molecules could be used as antimicrobial agents.

MATERIALS AND METHODS:

Antimicrobial activity of these compounds were determined by broth microdilution method reported by the Clinical and Laboratory Standards Institute (CLSI) against the bacteria (Escherichia coli ATCC 25922, Enterococcus faecalis ATCC 29212, Pseudomonas aeruginosa ATCC 27853, Staphylococcus aureus ATCC 29213) and the fungi (Candida albicans ATCC 90028, C. krusei ATCC 6258, C. parapsilosis ATCC 90018). Piperacillin/Tazobactam and Fluconazole used as control agents. pka value was calculated with potentiometric titration.

RESULTS:

CE2 was the most active compound against E. faecalis with a minimum inhibitory concentration (MIC) value of 64 (µg/mL). CE7 has a MIC value of 128 µg/mL against E. faecalis. Both CE2 and CE7 compounds has a MIC value of 512 µg/mL against S. aureus and E.coli. Moreover Both compounds have antimicrobial activity against P. aeruginosa with a MIC value of 256 µg/mL. Both compounds have an antifingal effect against C. albicans, C. parapsilosis and C. krusei (MIC values range between 256 and 512 µg/mL). pka values were calculated as 5,02 and 7,29 for CE2 and CE7, respectively.

CONCLUSIONS:

CE2 and CE7 have both antibacterial and antifungal effect. However the MIC values are high.

REFERENCES:

1. Westmark et al., (1994) J. Am. Chem. Soc.116: 9343-9344.
2. Clinical and Laboratory Standards Institute, Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically, Approved Standard 8th ed., M 07-A8. Clinical and Laboratory Standards Institute, Wayne, PA (2008).
3. Clinical and Laboratory Standards Institute, Reference method for broth dilution antifungal susceptibility testing of yeasts: approved Standard 3rd ed., M 27-A3. Clinical and Laboratory Standards Institute, Wayne, PA (2008).

P-027: ANTIBACTERIAL, ANTICHOLINESTERASE, A-AMYLASE AND A-GLUCOSIDASE INHIBITORY ACTIVITIES OF FERULAGO MUGHLAE PEŞMEN AND FERULAGO SANDRASICA PESMEN & QUÉZEL GROWING IN TURKEY

[1] Karakaya, S., [2] Bostanlik, F.D., [3] Koca, M., [4] Simsek, D., [5] Gozcu, S., [1] Yuca, H., [1] Ozbek, H., [2] Kılıc, C.S., [1] Guvenalp, Z., [4] Altanlar, N.

[1]Ataturk University, Department of Pharmacognosy, Erzurum, Turkey

[2]Ankara University, Department of Pharmaceutical Botany, Ankara, Turkey

[3]Ataturk University, Department of Pharmaceutical Chemistry, Erzurum, Turkey

4Ankara University, Department of Pharmaceutical Microbiology, Ankara, Turkey

5Erzincan University, Department of Pharmacognosy, Erzincan, Turkey

INTRODUCTION:

Ferulago species are used as anthelmintic, sedative and aphrodisiac, along with in salads or as seasoning for their special odors (1). The study reports the antibacterial, anticholinesterase, α-amylase and α-glucosidase inhibitory activities of essential oils (EOs) of fruits and extracts, fractions from roots and aerial parts and isolated compounds from CH2Cl2 fraction of roots from F. mughlea and F. sandrasica.

MATERIALS AND METHODS:

Antibacterial activities were carried out against S.aureus, E.coli, P.aeruginosa and B.subtilis by broth dilution methods (2). Anticholinesterase activity was assessed via Ellman's method (3), α-amylase and α-glucosidase inhibitory activities via methods reported in Karakaya et al., 2018 (4). Compounds' structures were elucidated by detailed analyses (NMR and MS).

RESULTS:

EOs and extracts showed antibacterial activity against all bacteria between 0.097-12.5 and 31.25-1000 µg/mL values, respectively. Activity of EOs were significant. The CH2Cl2 fraction of root from F. mughlae best inhibited AChE (48.55%) and the CH2Cl2 fraction of root from F. sandrasica best inhibited BuChE (97.09%). Felamidin showed significant α-glucosidase inhibitory activity (94.57%) when compared to the reference standard acarbose (50.81%). None of the samples were shown α-amylase inhibitory activity.

CONCLUSIONS:

Antibacterial activity of F. sandrasica EO, antioxidant and anticholinesterase activities of CH2Cl2 fraction of roots from F. mughlae and F. sandrasica promises hope to study on to be converted into a pharmaceutical product.

REFERENCES:

1. Erdurak CS (2003). Ankara University Doctorate Thesis, Ankara.
2. CLSI (2012). Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard-9th Edition. CLSI document M07-A9. Wayne, PA: Clinical and Laboratory Standards Institute.
3. Ellman GL, Courtney D, Andies V, Featherstone RM (1961). Biochem Pharmacol, 7:88-95.
4. Karakaya S, Gozcu S, Guvenalp Z, Ozbek H, Yuca H, Dursunoglu B, Kazaz, Kılıc CS (2018). Pharm Biol, 56(1):18-24.

P-028: ANTHELMINTIC ACTIVITY OF NIGELLA SATIVA AGAINST CAENORHABDITIS ELEGANS

[1] Sen, E., [2] Ogut, T., [3] Olgun, A., [4] Kisa, O.

[1] Altınbas University, Department of Biochemistry, Istanbul, Turkey

[2] Altınbas University, Faculty of Pharmacy, Istanbul, Turkey

[3]Istinye University, Faculty of Pharmacy, Istanbul, Turkey

4Altınbas University, Department of Pharmaceutical Microbiology, Istanbul, Turkey

INTRODUCTION:

Discovering new anthelmintic compounds from natural plants is important especially due to increasing resistance against classical anthelmintic drugs (1, 2). Nigella sativa (N. sativa), a medicinal plant, is used as antidiabetic, anticancer, immunomodulator, analgesic, antimicrobial, anti-inflammatory, spasmolytic, bronchodilator, hepato-protective, renal protective, gastroprotective, and antioxidant (3). However, seeds of N. Sativa extracts are slightly toxic against Caenorhabditis elegans (C. elegans) (4), a free living nematode that is used very commonly as a model organism. C. elegans has also been used to screen anthelmintic activity of plant extracts, because of its short life span, simple structure, and easy maintenance. In our study, we aimed to evaluate nematocidal activity of N. sativa by using C. elegans as a model.

MATERIALS AND METHODS:

Anthelmintic activity of N. sativa was evaluated by toxicity assays in C. elegans during its early larval and adult stages. Different concentrations of N. sativa oil (900, 450, 270 and 0 mg/mL) were tested, and Levamisole (2,5 mg/ml) was used as positive control. The toxicity assessments were done under stereomicroscope after 24, 48 and 72 hours from the start of treatments. The number of survived nematodes was counted for lifespan (survival) analyses every day. This evaluation was performed for both larval

and adult stage worms. Statistical significance was assessed with Student T-test ($p < 0.05$).

RESULTS:

This study showed that N. sativa essential oil significantly decreases lifespan/survival of adult C. elegans in both larval and adult stages after 24 hours just when N. sativa was used at 900mg/mL final concentration. After 48 and 72 hours, the number of live adult animals in treatment group significantly decreased compared with untreated control group. Additionally, larval stage worms were more sensitive to N. sativa essential oil than the adults.

CONCLUSIONS:

This study demonstrates anthelmintic and toxic activities of N. sativa essential oil against both larval and adult worms. Larval animals were more sensitive than adults. We recommend further studies on other effects of N. sativa on C. elegans after removing toxic compound(s) from the extract.

REFERENCES:

1. Geerts S, Gryseels B (2000). Clinical Microbiology Reviews, 13: 207–222.
2. Waterman C et al., (2010). Journal of Ethnopharmacology, 127: 755–759.
3. Aftab A et al., (2013). Asian Pac J Trop Biomed, 3(5): 337-352.
4. Ali BH, Blunden G (2003). Phytotherapy Research, 17: 299-305.

P-029: DETERMINATION OF LACTIC ACID CONTENT OF A LACTIC ACID BACTERIUM BY HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

[1] Kiymaci, M.E., [2] Gumustas, M., [1] Altanlar, N.,[1] Akin, A., [3] Zenciroglu, A., [4] Ozkan, S.A.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Ankara, Turkey

[2]Ankara University, Institute of Forensic Sciences, Department of Forensic Toxicology, Ankara, Turkey

[3]Ankara Dr. Sami Ulus Obstetrics and Gynecology, Children Health and Diseases Training and Research Hospital, Department of Neonatology, Ankara, Turkey

4Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

The aim of this study was to develop and optimize a selective high-performance liquid chromatography method for the determination and validation of Pediococcus acidilactici strain's lactic acid content. Also to determine the antimicrobial activity of tested strain against different bacterial ATCC standards.

MATERIALS AND METHODS:

Antimicrobial activity of P. acidilactici strain against standard test microorganisms was determined by the spot lawn method and the quantitation of its lactic acid was carried out by high performance liquid chromatography on a Rezex ROA organic acid (300x7.8 mm) analytical column.

RESULTS:

The lactic acid amount of the P. acidilactici strain was found in the range between 5.59 - 5.94 mg mL-1 and the strain was able to inhibit the growth of Pseudomonas aeruginosa ATCC PAO-1, Pseudomonas aeruginosa ATCC 27853, Pseudomonas aeruginosa ATCC 9027, Enterococcus faecalis ATCC 29212 by its lactic acid content.

CONCLUSIONS:

This study explains a simple, selective, and fully validated procedure for the determination of lactic acid from lactic acid bacteria.

ACKNOWLEDGEMENTS:

This study was supported by "Ankara University Scientific Research Projects Coordination Unit" under the project number: 14L0237003.

P-030: ENZYME INHIBITORY EFFECT OF IBERIS SEMPERVIRENS EXTRACTS

Zengin, G. Aktumsek, A

Selcuk University, Faculty of Science, Department of Biology, Konya, Turkey

INTRODUCTION:

Nowadays, knowledge of ancient botanical medicinal practices and application of modern phytochemical techniques have provided the excellent tools for the purification and structural elucidation of various phyto-compounds, which, in turn, has given insights into their mode of action on the human body (1). This study has been designed to investigate for the first time the effects of the ethyl acetate, methanolic, and water extracts of Iberis sempervirens on key enzymes.

MATERIALS AND METHODS:

Plant material was collected during the flowering period in 2015 from Adana, Turkey (between Pozantı and Camlibel village). The methanol, ethyl acetate, and water extracts were prepared from Iberis sempervirens. The total phenolic and flavonoid content were determined using colorimetric methods. Enzyme inhibitory properties were detected against cholinesterase, tyrosinase, α- amylase and α-glucosidase.

RESULTS:

The ethyl acetate extract was more potent against cholinesterases (1.93 mgGALAE/g extract for AChE and 1.99 mgGALAE/g extract for BChE)

and α-amylase (0.81 mmolACAE/g extract), while the methanol extract were most active against α-glucosidase (7.69 mmolACAE/g extract). The water extract was also exhibited notable inhibitory activity against tyrosinase (5.25 mgKAE/g extract).

CONCLUSION:

The present findings suggest that Iberis sempervirens can be considered as a potential source of bioactive compounds for novel phytopharmaceuticals development in the treatment and/or management of noncommunicable diseases.

REFERENCES:

1. Khan ZR, Moni F, Sharmin S, Al-Mansur MA, Gafur A, Rahman O, Afroz F (2017). Pharmacology & Pharmacy 8, 253.

P-031: ANTIOXIDANT PROPERTIES OF LOTUS AEGAEUS EXTRACTS

Zengin, G. Aktumsek, A

Selcuk University, Faculty of Science, Department of Biology, Konya, Turkey

INTRODUCTION:

Plant secondary metabolites have been used for ages in folk medicine due to their known pluripotential biological attributes. Nowadays, they are regarded as valuable sources of bioactive compounds used in the development of pharmaceutics, cosmetics, fine chemicals, or recently as nutraceuticals (1,2). This study has been designed to investigate for the first time the antioxidant effects of the ethyl acetate, methanolic, and water extracts of Lotus aegaeus.

MATERIALS AND METHODS:

Lotus aegaeus was collected during the flowering period in 2015 from Konya (Balcılar, Taskent). The methanol, ethyl acetate, and water extracts were prepared for antioxidant ability. The antioxidant abilities of the investigated extracts were tested using different assays including free radical scavenging, reducing power, phosphomolybdenum, and metal chelating. The total phenolic and flavonoid content were also determined using colorimetric methods.

RESULTS:

All the extracts showed strong antioxidant abilities. The water extract exhibited the strongest free radical scavenging ability on both DPPH (37.90 mgTE/g extract) and ABTS (101.30 mgTE/g extract). The ethyl acetate extract had the greatest cupric reducing power (72.88 mgTE/g extract). However, the water extract had good metal chelation ability (14.91 mgEDTAE/g extract).

CONCLUSION:

L. aegaeus showed potent biological attributes, which advocates for further studies to explore its potential use as active phytopharmaceuticals.

REFERENCES:

1. Atanasov AG, Waltenberger B, Pferschy-Wenzig EM, Linder T, Wawrosch C, Uhrin P, Temml V, Wang, L, Schwaiger S, Heiss EH. (2015). Biotechnology Advances 33:1582-1614.
2. Balandrin MF, Klocke JA, Wurtele ES, Bollinger WH. (1985). Science 228:1154-1160.

P-032: PHYTOCHEMICAL STUDIES ON SESELI PETRAEUM M. BIEB. (APIACEAE)

Onder, A., Cinar, A.S.

Ankara University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

The Apiaceae is well-known flowering plant family. Seseli L. is one of the Apiaceae genus, annual or biennial herbaceous plants (1, 2). So far, various phytochemical studies on Seseli species showed that these plants contain particularly coumarins, cinnamic acid derivatives, sesquiterpene lactones, phenylpropanoids and essential oils (3-5). The subject of this work is to the determination of the coumarins by chromatographic methods from Seseli petraeum M. Bieb. growing in a small place in Black Sea Coastal Region.

MATERIALS AND METHODS:

The plant was collected from the roadside cliffs in Trabzon. The extracts with different polarities (n-hexane, ethyl acetate, and methanol) were obtained from both parts using Soxhlet apparatus. Then all extracts were applied to TLC (Thin Layer Chromatography). On the other hand, the n-hexane extract has been subjected to CC (Column Chromatography).

RESULTS:

Thin Layer Chromatography (TLC) experiments were carried out by 6 types of extracts (from aerial parts and roots). In addition, the n-hexane extract of the roots of S. petraeum L. have been subjected to column chromatography, and 10 fractions were obtained at the end, together with pure pyranocoumarin type coumarins (A and B).

CONCLUSIONS:

In the present study, the chromatographic profile obtained by TLC have been clarified and given by the photos. The tentative structures of the pyranocoumarins will be given all details in future studies. Moreover, the results showed that the coumarins are rich in S. petraeum. The fractions had a strong potential for the isolation of other coumarinic type compounds. The study has been focused not only isolation but also the chromatographic profile of the species were also clarified.

ACKNOWLEDGMENTS

This study has been supported by a grant of Ankara University Scientific Research Projects (BAP) Coordinator-18L0237002.

REFERENCES:

1. Hedge IC, Lemond JM (1972). Seseli L. In Flora of Turkey and The East Aegean Islands Ed.: P. H. Davis, Vol 4, Edinburgh, Edinburgh University Press, p: 367-372.
2. Dioscorides, (2002). In: De Materia Medica. Codex Neapolitanus Graecus 1 of the National Library of Naples, Militos Press, Athens, 215 pp.
3. Barrero AF, Herrador MM, Arteaga P (1992). Phytochemistry. 31:203-207.
4. Murray RDH, Mendez J, Brown SA (1982). In: The Natural Coumarins, Occurrence, Chemistry and Biochemistry, John Wiley & Dond Ltd., New York.
5. Kupeli E, Tosun A, Yesilada E (2006). J. Ethnopharm,104: 310-314.

P-033: CHEMICAL COMPOSITION OF THE ESSENTIAL OIL FROM THE FRUITS OF SESELI PETRAEUM M. BIEB. (APIACEAE)

[1] Onder, A., [1] Cinar, A.S., [2] Carbonell Barrachina, A.A.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

[2]Universidad Miguel Hernández de Elche, Department of Agro-Food Technology, Alicante, Spain

INTRODUCTION:

Seseli L. from Apiaceae family (1) comprises coumarins, terpenoids, and essential oils. The genus has been exhibited antimicrobial, antioxidant, antipyretic, anti-inflammatory, and many other important activities. The studies on its phytochemical constituents and biological activities are very limitedly performed (2, 3). There are several studies on volatile oils of Seseli species (3). It is necessary to emphasize that the Seseli species are very important for their phytoconstituents and effects. Therefore, in this study, it is aimed to clarify the essential oil composition of Seseli petraeum M. Bieb. called as Stone Seseli, Taş Seseli, Taş Çaşırı), which grows in a narrow part of the Black Sea coastal region in Turkey.

MATERIALS AND METHODS:

The fruits of the plant was roughly crushed. The crashed fruits were subjected to hydro-distillation in the Clevenger apparatus for 3 hours. The oil was analyzed by Gas Chromatography (GC) and Gas Chromatography/Mass spectroscopy (GC/MS).

RESULTS:

The volatile oil was obtained by the yield of 1.5-2% from the fruits of the plant (65 g). The major components have been determined as carotol (17.25%), γ-terpinene (10.73%), p-cymene (7.93%), germacrene-D (7.65%), trans-β-ocimen (7.31%), and β-farnesene (8.50%).

CONCLUSION:

In the present study, the essential oil composition of Seseli petraeum M. Bieb. has been determined by GC/MS. The most dominant compound has been found as carotol (17.25%) which is the most significative constituents of the other Seseli species. In the end, it is understood that the volatile oil is rich in sesquiterpenoids.

ACKNOWLEDGEMENTS:

This study has been supported by a grant of Ankara University Scientific Research Projects (BAP) Coordinator-18L0237002.

REFERENCES:

1. Davis PH, Mill RR, Tan K (1988). Flora of Turkey and the East Aegean Islands, Edinburgh University Press, Edinburgh, 10: 265-267.
2. Kupeli E, Tosun A, Yesilada E (2006). J. Ethnopharm.104: 310-314.
3. Tosun A, Kurkcuoglu M, Dogan E, Duman H, Baser KHC (2006). Flavour Frag J. 21: 257-259.

P-034: CRANBERRY EXTRACT ELICITS THE RELAXATION IN RAT CORPUS CAVERNOSUM TISSUE

[1] Onder, A, [2] Gur, S, [2,3] Yilmaz Oral, D

[1]Ankara University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Pharmacology, Ankara, Turkey

[3]Cukurova University, Faculty of Pharmacy, Department of Pharmacology, Adana, Turkey

INTRODUCTION:

Cranberry (Vaccinium macrocarpon) from Ericaceae family grows in Eastern North America. Cranberry displays several biological activities such as antioxidant, anticancer, etc. due to mostly phenolic contents. Various cranberry forms (juice, tablets, capsules, and syrup) have been used widely for many years for the management of urinary tract infections (UTIs) (1,2). Although effects of cranberry products may have a beneficial effect on the erectile dysfunction (ED) (3), the scientific evidence is limited.

MATERIALS AND METHODS:

Male Sprague-Dawley rats (n=8) were used in this study. We evaluated the effects of one of the dietary supplements present in the market, containing concentrated extract of cranberry fruit-(E) on rat corpus cavernosum (CC). After phenylephrine (Phe, 10 μM) contraction, the relaxant responses were determined in the presence of some inhibitors.

RESULT:

The relaxant responses of rat CC strips were observed in the presence or the absence of cranberry-E. Cranberry-E induced relaxation of rat CC (maximum response: 76.1±3.6%) after Phe-contraction. Cranberry-E evoked long-lasting relaxations. The nitric oxide synthesis inhibitor N(omega)-nitro-L-arginine methyl ester (L-NAME; 10 μM), the soluble guanylate cyclase inhibitor ODQ (10 μM), and endothelial disruption all failed to affect the relaxations. The relaxant responses to acetylcholine (10 μM), electrical field stimulation (10 Hz), and sodium nitroprusside (0.01 μM) in rat CC were increased after incubation with cranberry-E. The results of the current study could be used by physicians to recommend cranberry extract ingestion to decrease the incidence of ED patients with UTI as an alternative therapy.

CONCLUSION:

The underlying mechanism of cranberry products is likely independent of the nitric oxide-cyclic guanosine monophosphate pathway. Overall, these in vitro studies suggested that consumption of cranberry-E may be efficient and represent an exciting new strategy to prevent and diminish ED in men.

REFERENCES:

1. Jeszka-Skowron M, Zgoła-Grzes´kowiak A, Stanisz E, Was´kiewicz A. (2017). Food Chemistry 221:228–236.
2. Bukhari S, Chiragh S, Tariq S, Alam MA, Wazir MS, Suleman M. (2015). J Ayub Med Coll Abbottabad. 27(3):660-3.
3. Stasiak M, Żarłok K, Tomaszewski W.(2016). Wiad Lek.69:576-581, 2016.

P-036: IN VITRO EFFECTS OF FLUOROQUINOLONE ANTIBIOTICS ON PROBIOTICS

[1] Cimik, A., [2] Demirci, F.

[1] Anadolu University, Faculty of Pharmacy, Eskişehir, Turkey

[2] Anadolu University, Faculty of Pharmacy, Deparment of Pharmacognosy, Eskişehir, Turkey

INTRODUCTION:

Fluoroquinolones are a popular group of snythetic antibiotics with a broad antibacterial spectrum showing a good distribution in tissues (1). However, this type of compounds were shown to have a high likelihood of overuse as well as side effects such as neuropathy and psychiatric disorders (2). In this present study, it was aimed to determine the in vitro activity of fluoroquinolones on ten different probiotic microorganisms, which are thought to have a positive effect on neuropathy and psychiatric disorders especially associated with endogenous acetyl choline secretion (3).

MATERIALS AND METHODS

Three quinolones were evaluated by using the microdilution method against probiotic bacteria and yeast, where ketoconazole and chloramphenicol was used as control group.

RESULTS:

The MIC values (μg/mL) of the quinolones

Microorganisms	Ciprofloxacin	Levofloxacin	Moxifloxacin	Ketoconazole	Chloramphenicol
Bacillus subtilis var. clausii ATCC-9799	25	<1.56	6.25	<0.16	<0.16
B.subtilis var. natto BN	6.25	<1.56	6.25	2.5	0.31
Streptococcus thermophilus TH-4	100	<1.56	<1.56	5	1.25
S. salivarius K12	6.25	50	>800	0.16	0.15
Lactobacillus acidophilus La-14	6.25	<1.56	<1.56	2.5	1.25
L. reuterii DSM 17938	6.25	<1.56	<1.56	2.5	1.25
L. rhamnosus GG	6.25	<1.56	<1.56	2.5	1.25
Bacillus coagulans SNZ 1969	6.25	1.56	1.56	2.5	1.25
Saccharomyces cerevisae ATCC - MYA9763	400	200	800	<0.16	>80
S. cerevisae var. boulardii ATCC - MYA976	>800	>800	>800	5	>80

CONCLUSIONS:

According to this study, levafloxacin and ciprofloxacin were more effective at lower concentrations on probiotic microorganisms compared to moxifloxacin. S. thermophilus was the most resistant bacterium when compared to ciprofloxacin. S. salivarius was the most resistant bacterium compared to moxifloxacin and levafloxacin. It was also observed that S. boulardii was the most resistant yeast against fluoroquinolones. Ciprofloxacin can be safely used in the concentration range in which L. acidophilus is thought to be effective. The standard antifungal ketokonazole showed growth inhibition against the probiotics except S.c. var. boulardii. The standart antibacterial agent chloramphenicol showed inhibitory activity against the bacteria at reasonable concentrations. The incidence and prevalence of neuropathy and psychiatric disorders may be reduced in the endogenous acetylcholine metabolism in humans as previously reported (3). Further detailed work is on going.

REFERENCES

1. Yakupoğulları, Y., Gündüz, A., Özcan, M., Doğukan, M., Seyrek, A., & Yılmaz, M. (2014). Fırat Tıp Dergisi 11, 45.
2. Anonymous. US Food and Drug Administration. (2013). FDA drug safety communication: FDA

requires label changes to warn of risk for possibly permanent nerve damage from antibacterial fluoroquinolone drugs taken by mouth or by injection. UCM365078.

3. Horiuchi Y., Kimura R., Kato N et al. (2003). Life Sci 72, 1745.

P-037: ANTIMICROBIAL ACTIVITY POTENTIAL OF SOME SPICES MARKETED IN TURKEY

[1] Akay, BK, [1] Onder, A, [2] Gurpinar, SS, [2] Eryilmaz, M

1Ankara University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

2 Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Ankara, Turkey

INTRODUCTION:

Spices are a part of the plants used for many purposes as colorants, preservatives, or medicines (1,2). The objective of this study was to evaluate to the potential antimicrobial activity of some spices from Apiaceae family such as Amni visnaga (Diş otu, Hıltan), Anethum graveolens (Dereotu), Apium graveolens (Kereviz), Coriandrum sativum (Kişniş), Cuminum cyminum (Kimyon), Daucus carota (Havuç), Foeniculum vulgare (Rezene), Petroselinum sativum (Maydanoz), Pimpinella anisum (Anason).

MATERIALS AND METHODS:

The spices have been extracted by n-hexane in a reflux. After that, all extracts have been subjected to Thin Layer Chromatography to examine their chromatographic profile. Then, the n-hexane extracts were screened for their potential in vitro antibacterial activity against Staphylococcus aureus ATCC 29213, Enterococcus faecalis ATCC 29212, Escherichia coli ATCC 25922, Klebsiella pneumoniae ATCC 13883, Pseudomonas aeruginosa ATCC 27853 and antifungal activity against Candida albicans ATCC 10231. Microbroth dilution method was used for determination of the minimum inhibitory concentrations (MIC) [3,4]. Serial two-fold dilutions ranging from 10 to 0.078 mg/mL were prepared in the medium. A set of wells containing only inoculated broth, 10% DMSO, ampicillin, ofloxacin, ciprofloxacin, and fluconazole were used as a control.

RESULTS:

Coriandrum sativum, Anethum graveolens, Daucus carota and Pimpinella anisum did not show antimicrobial activity against test microorganisms. Except these, extracts possessed activity having MIC values of 2.5-5-10 mg/mL against the tested microorganisms

CONCLUSION:

The extracts showed antimicrobial activity for their nonpolar components which are accumulated to the hexane. Therefore, spices may have a great potential to be developed as new and safe antimicrobial agents.

ACKNOWLEDGMENTS

The spices were supplied by Mısır Çarşısı Baharat İth. İhr. Ltd. Şti.

REFERENCES:

1. Liu Q, Meng X, Li Y, Zhao CN, Tang GY, Li HB (2017). Int J Mol Sci. 18:1-62.

2. Jessica Elizabeth T, Gassara F, Kouassi AP, Brar SK, Belkacemi K (2017). Crit Rev Food Sci Nutr. 57:1078-1088.

3. European Committee on Antimicrobial Susceptibility Testing (EUCAST). Breakpoint tables for interpretation of MICs and zone diameters. Version 3.1., Valid from 2013-02-11.

4. Clinical Laboratory Standards Institute (CLSI) M100-S23; Vol. 33 No.1, January 2013 3 ISO Standart 20776-1, 2006.

P-038: ANIOXIDANT ACTIVITY OF LYCIUM BARBARUM L. CULTIVATED IN TURKEY.

Heydari, H., Konuklugil, B.

Ankara University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

In this study the antioxidant activity of Lycium barbarum L. was determined. The fruits of L. barbarum L. (Solanaceae), have wide range of pharmacological activities. The major bioactive compounds of L. barbarum are polysaccharides, flavonoids, carotenoids and phenolic acids, which mainly account for immunomodulatory and antioxidant activities (1). L. barbarum L. also known as wolfberry, goji berry has been used as a preventative and curative agent for thousands of years (2). Free radicals are known to be the main cause of aging, heart disease, stroke, diabetes mellitus, cancer and rheumatism (3). The fruits of L. barbarum L. are rich of polysaccharides that had significant free radical-scavenging activity (4).

MATERIALS AND METHODS:

L. barbarum L. was obtained from Temmuz Organik Üretim Çiftliği Konya. 100g of dried fruit L. barbarum L. were grinded and extracted by different solvents; methanol, 70% methanol and 70% acetone. The extracts were dried under vacuum. Different concentrations of extracts were attempted to evaluate the antioxidant activity by DPPH and superoxide radical scavenging methods and the IC50 of the extracts were calculated (5). Ascorbic acid and quercetin were used as standards.

RESULTS:

According to the results of DPPH and superoxide radical scavenging methods 70% aseton extract (IC50: 2.2 ± 1.3 mg/ml) was shown better antioxidant activity than the metanolic and 70% metanolic extracts (IC50: 2.6 ± 1.4 mg/ml).

CONCLUSIONS:

In conclusion, the present study demonstrated that Turkish L. barbarum L. fruits have sufficient antioxidant activity such as Chinese samples. L. barbarum L. could use as a potential source of natural antioxidant. Further studies will be continue to identify the active compound/s responsible for antioxidant activity.

ACKNOWLEDGEMENTS:

The material of this study was obtained from Temmuz Organik Üretim Çiftliği Konya.

REFERENCES:

1. Lam S, Luo Z, Wu D, Cheong K, Hu D, Xia Z, Zhao J, Li S (2016). Journal of Food Science, 81:1378-1384.
2. Wang Y, Zhao H, Sheng X, Gambino P, Costello B, Bojanowski K (2002). Journal of Ethnopharmacology, 82:169-175
3. Wu S, Ng L, Lin C (2004). Phytotherapy Research, 18:1008–1012
4. Li XL, Zhou AG (2007). Medicinal Chemistry Research, 15:471–482.
5. Shirwaikar A, Shirwaikar A, Rajendran K, Punitha IS (2006). Biological and Pharmaceutical Bulletin, 29:1906–1910.

P-039: STANDARDIZATION OF THE ETHYL ACETATE EXTRACT FROM QUERCUS MACRANTHERA SUBSP. SYSPIRENSIS

[1] Dursunoglu, B., [1] Yuca, H., [2] Gozcu, S., [1] Guvenalp, Z.

[1] Ataturk University, Faculty of Pharmacy, Department of Pharmacognosy, Erzurum, Turkey

[2] Erzincan University, Faculty of Pharmacy, Department of Pharmacognosy,Erzincan, Turkey

INTRODUCTION:

The genus Quercus is represented with 24 species and 15 subspecies in Turkish flora. Quercus macranthera subsp. syspirensis (Fagaceae) is an ecologically important endemic species and known as İspir oak (1). It contains some phenolic compounds such as tannins in its shell (2). In our previous study, α-glucosidase inhibitory activity of ethyl acetate extract from fruits of this plant was determined. In the present study, performing the qualitative and quantitative analysis of active compounds in ethyl acetate extract by HPLC method and preparing the standardized extracts based on the α-glucosidase inhibition were aimed.

MATERIALS AND METHODS:

In the present study, rapid, precise and accurate HPLC methods have been developed and validated for epigallocatechin gallate (EGCG), epigallocatechin (EGC), epicatechin gallate (ECG) and catechin (C) in ethyl acetate extract obtained from fruits of Q. macranthera subsp. syspirensis. In vitro α-glucosidase inhibitory activities were investigated according to the method of Tao et al., 2013 (3).

RESULTS:

α-Glucosidase inhibitory activities of active compounds have found as EGCG > ECG > EGC > C. Their IC50 values were determined as 0.0235, 0.0519, 0.2409, and 0.3401 mg/ml, respectively. The concentrations of ECG, EGCG, C and EGC in ethyl acetate extract (10 mg/ml) were found 0.717, 0.270, 0.0813 and 0.004%, respectively.

CONCLUSIONS:

Catechins-enriched standardized ethyl acetate extract has the best α-glucosidase inhibitory activity.

ACKNOWLEDGEMENTS:

This study was supported by The Foundation of Ataturk University (2016/121). Benan Dursunoglu would like to acknowledge the scholarship during her postgraduate program provided by the Turkish Scientific and Technical Research Council (TUBITAK).

REFERENCES:

1. Güner A, Aslan S, Ekim T, Vural M, Babaç MT (2012). In: Turkiye Bitkileri Listesi (Damarlı Bitkiler), Nezahat Gokyigit Botanik Bahcesi Yayınevi. İstanbul, pp 506-511.
2. McCue P, Kwon YI, Shetty K (2005). Journal of Food Biochemistry, 29(3):278-294.
3. Tao Y, Zhang Y, Cheng Y, Wang Y (2013). Biomedical Chromatography, 27:148-155.

P-040: ANATOMY OF ANCHUSA AZUREA MILLER (BORAGINACEAE)

Dursunoglu, B., Karakaya, S., Guvenalp, Z.

Ataturk University, Department of Pharmacognosy, Erzurum, Turkey

INTRODUCTION:

The genus Anchusa L. (Boraginaceae) is mainly distributed along the Mediterranean coast, Africa, Europe and Western Asia that is represented with about 35 species (1). There are 15 species of the genus Anchusa found in Turkey (2). A. azurea is used traditionally as stimulant, tonic, demulcent, diuretic and for fever, cough and wound healing (2, 3). It contains pyrrolizidine alkaloids, flavonoids, triterpene saponins, fatty acids, phenolic acids and

polysaccharides (2, 3). Anticancer, antioxidant, antiviral and anti-inflammatory activities of A. azurea were reported in the literature (3).

MATERIALS AND METHODS:

The plant was collected from Erzurum (Turkey) in 2017. Specimens were dried according to standard herbarium techniques and stored in the Herbarium of Atatürk University, Faculty of Pharmacy. The materials for anatomical study were preserved in 70% alcohol. Characteristic elements of stem, leaf and petiole were identified with preparing the sections and their structures were illustrated with photographs.

RESULTS:

The leaf is monofacial and stomata were located in the upper and lower leaf epidermises. The trichomes were observed in the leaf and stem of A. azurea. The secretory channels were located in the stem. The petiole anatomy of A. azurea was similar to anatomy of the stem.

CONCLUSIONS:

In the present study, anatomical structures of the stem, petiole and leaf of A. azurea were investigated. The anatomical properties given in this study provide description of A. azurea. Our results should be useful in future studies about this genus.

ACKNOWLEDGEMENTS:

Benan Dursunoglu would like to acknowledge the scholarship during her postgraduate program provided by the Turkish Scientific and Technical Research Council (TUBITAK).

REFERENCES:

1. Chen KK, Xie ZJ, Dai W, Wang Q (2017). Natural Product Research, 31:959-965.
2. Kuruuzum-Uz A, Suleyman H, Cadirci E, Guvenalp Z, Demirezer LO (2012). Zeitschrift für Naturforschung, 67c:360-366.
3. Al-Snafi AE (2014). International Journal of Pharmacy and Pharmaceutical Sciences, 6:7-10.

P-041: ANATOMY OF EPILOBIUM ANGUSTIFOLIUM L. (ONAGRACEAE)

[1] Akcil, B., [2] Karakaya, S., [2] Guvenalp, Z.

[1]Erzincan University, Department of Pharmacognosy, Erzincan, Turkey

[2]Atatürk University, Department of.Pharmacognosy, Erzurum, Turkey

INTRODUCTION:

The genus Epilobium belongs to Onagraceae family and represented with 21 species in Turkey (1). One of these species, E. angustifolium, is an annual plant so green leafy, flowering with a height of 0.5-3 m (2) which known as “yakı otu” in our country (1). The infusion prepared from the plant is used for migraine, insomnia, anemia, delirium, infections and colds in folk medicine (3). Its usage in the treatment of mucous membrane lesions is also reported (4). The plant contains polyphenolic compounds such as flavonoids, phenolic acids and ellagitannins (3).

MATERIALS AND METHODS:

The plant was collected from Erzurum City Forest (Turkey) in September 2017. Specimens were dried and stored in the Herbarium of Atatürk University, Faculty of Pharmacy. The materials for anatomical study were preserved in 70% alcohol. In this study, anatomical structures of the characteristic elements from the stem, leaf, sepal, petal, anther, and filament of E. angustifolium were identified with taking the sections. Their structures were illustrated with photographs.

RESULTS:

Leaf is bifacial which located stoma in the lower epidermis. Very dense and unicellular trichome (only stem, leaf, petiole) and abundant cluster crystals of calcium oxalate were shown in sections of stem, leaf, petiole and petal. Thin short and thick long raphides were shown all over the leaf. Trichomes with single cell and glandular hair with a unicelular stalk and secretory head were found at sepal anatomy which was similar to petal.

CONCLUSIONS:

In the present study, anatomical structures of the stem, leaf, sepal, petal, anther and filament of E. angustifolium were investigated. The anatomical properties given in this study provide description of E. angustifolium. Our results should be useful in future studies about this genus.

ACKNOWLEDGEMENTS:

Bilge AKCIL would like to acknowledge the scholarship during her postgraduate program provided by the Turkish Scientific and Technical Research Council (TUBITAK).

REFERENCES:

1. Güner A (2012). In: Türkiye Bitkileri Listesi (Damarlı Bitkiler), pp 627-629
2. Myerscough PJ, Whitehead FH (1966). New Phytologist, 65: 192-210
3. Schepetkin IA, Ramstead AG, Kirpotina LN, Voyich JM, Jutila MA, Quinn MT (2016). Phytotherapy Research, 30:1287-1297.
4. Ruszova E, Cheel J, Pavek S, Moravcova M, Hermannova M, Matejkova I, Spilkova J, Velebny V, Kubala L (2013). Gen. Physiol Biophys, 32: 347-359.

P-042: COMPARISON OF ALPHA-GLUCOSIDASE INHIBITORY AND ANTIOXIDANT ACTIVITIES OF DIFFERENT SUMAC PRODUCTS

[1] Akcil, B., [2] Sevindik, H.G., [2] Yuca, H., [1] Gozcu, S., [2] Guvenalp, Z.

[1] Erzincan University, Faculty of Pharmacy, Department of Pharmacognosy, Erzincan, Turkey

[2] Ataturk University, Faculty of Pharmacy, Department of Pharmacognosy, Erzurum, Turkey

INTRODUCTION:

Rhus coriaria L. belongs to Anacardiaceae family which is commonly known as “sumac”. Mature fruits are used as spice and to prepare sumac sauce (1). This plant is one of the export products of Turkey. Sumac is used as hemostatic, antiseptic and constipating agent in traditional medicine (2). Previous studies have shown that Rhus coriaria has anti-fungal, antibacterial, antioxidant, hypoglycemic and DNA protective effects (1). The aim of our study is to compare the activity of 3 different products obtained from this plant.

MATERIALS AND METHODS:

Three different products were the naturally mature fruits of the sumac plant (M), commercial spice (C) and commercial sauce (S). Antioxidant activity was determined by ABTS•+ (3) and DPPH• (4) scavenging activity, and antidiabetic activity by alpha-glucosidase inhibitory activity assay (5).

RESULTS:

In the ABTS•+ scavenging activity trolox (TR) was used as standard, the extract of the naturally collected sumac fruits (M) showed highest activity compared to commercial spice (C) and sauce (S) [TR>M>C>S (13.5>11.0>7.0>0%; 5 µg/ml)]. The results of the DPPH• scavenging activity are similar to those of the ABTS•+ test. Sumac fruit collected from the nature and commercial spice were found to be more active than the standard compound α-tocopherol (TK) [M>C>TK>S (21.5>11.8>11.1>3.2%; 10 µg/ml)]. In the alpha-glucosidase inhibitory activity assay, all samples showed higher inhibition effect than acarbose (A) used as standard [M>C>S>A (97.4>93.2>29.3>0.5%; 50 µg/ml)].

CONCLUSIONS:

We conclude that the sumac fruits are very effective on alpha-glucosidase inhibitory activity, but commercial spices and sauces are not as effective as naturally collected sumac.

ACKNOWLEDGEMENTS:

Bilge AKCIL would like to acknowledge the scholarship during her postgraduate program provided by the Turkish Scientific and Technical Research Council (TUBITAK).

REFERENCES:

1. Shabbir A (2012). The Journal of Animal & Plant Sciences, 22(2):505-512.

2. Baytop T (1999). In:Türkiye’de Bitkiler ile Tedavi-Geçmişten Bugüne. Nobel Tıp Basımevi: Istanbul.

3. Re R, Pellegrini N, Pannala A, Yang M (1999). Free Radical Biology & Medicine, 26:1231-1237.

4. Blois MS, (1958). Nature, 181:1199-1200.

5. Tao Y, Zhang Y, Cheng Y, Wang Y (2013). Biomedical Chromatography, 27:148-155.

P-043: ANTIMICROBIAL ACTIVITIES AND FATTY ACID COMPOSITIONS OF KUMQUAT, LIMEQUAT AND MEXICAN LIME SEEDS

Agalar, HG.,Temiz, B.,Ozturk, G.,Demirci B., Kirimer N.

Anadolu University, Faculty of Pharmacy, Department of Pharmacognosy, Eskişehir, Turkey

INTRODUCTION:

Citrus fruits are of great economic importance because of their in nature consumption and varies industrial applications. The wastes of these industries such as peels, seeds and pulps represent about 50% of the raw processed fruit. Large amounts of citrus seeds are discharged at the processing plants. This not only wastes a potentially valuable resource, but also aggravates already serious disposal problems (1). Therefore, in the present study, the seeds of small citrus fruits were evaluated for their potential antimicrobial activities and fatty acid compositions.

MATERIALS AND METHODS:

Mature Kumquat, Limequat and Mexican lime fruits were harvested from Subtropical Fruits Research and Development Center at Çukurova University, Adana in December, 2017. The seeds separeted from the fruits were dried. Each seed oil was extracted with n-hexane for 8 h using a Soxhlet apparatus. The solvent was then evaporated under reduced pressure at 40^{o}C. Fatty acids in all fixed oils were methylated by BF3. The fatty acid compositions were analyzed by GC-FID and GC-MS systems, simultaneously. The fixed oils were evaluated for their potential antimicrobial activity by CLSI M7-A7 method. Escherichia coli NRRLB-3008, Pseudomonas aeruginosa ATCC 27853, Salmonella typhimurium ATCC 13311, Bacillus cereus NRRL-B3711 and Streptococcus sanguinis ATCC 10556 were used as test microorganisms. Ciprofloxacin was used as a positive control.

RESULTS:

The seed oils yields of kumquat, limequat and mexican limes were calculated as 4.0%, 5.4%, 35.8%,respectively. Palmitic acid (52.3%), oleic acid (26.4%) and stearic acid (8.6%) were the major fatty

acids of kumquat seed oil; palmitic acid (35.4%), oleic acid (26.4%) and linoleic acid (17.5%) were the major in limequat seed oil; linoleic acid (35.5%), palmitic acid (25.4%), oleic acid (19.8%) were the major in mexican lime seed oil. Limequat seed oil showed noticable antimicrobial effect against P.aeruginosa ATCC 27853 and B.cereus NRRL-B3711 at 52 µg/mL (MIC) concentration.

CONCLUSIONS:

Limequat seed oil can be used as antimicrobial agent for lipophilic formulations. Extensive further studies were planned by our group.

REFERENCES:

1. Juhaimi FAL, Matthaus B, Ozcan MM, Ghafoor K (2016). Zeitschrift für Naturforschung, 71:79-85.

P-044: NEW HPLC METHOD FOR THE PHARMACOPOEIA ANALYSIS OF VIOLA HERBA CUM FLORE

Ergene Oz, B., Bahadir Acikara, O., Ozbilgin, S.,Ileri, H.K., Saltan Iscan, G.

Ankara University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

Viola tricolor L. and Viola arvensis Murray which are widely grown in Europe and Asia, belong to the Violaceae family and the aerial parts of the plants are used as folk medicine for several purposes such as diuretic, laxative, antirheumatismal effects and against skin disorders (1-3). The monograph of dried flowering aerial parts of V. tricolor and V. arvensis is documented as Viola herba cum flore in European Pharmacopoeia (EP 11.0). In this monograph, a spectrophotometric method is conducted to determine the total flavonoid content expressed as violanthin. The aim of this study was to develop a new method for the assay of Viola Herba cum Flore.

MATERIALS AND METHODS:

A gradient solvent system consisting of acetonitrile and water containing 0.02% o-phosphoric acid is used for the analysis. Besides, system suitability tests (resolution, capacity factor, tailing factor, theoretical plate number, linearity, reproducibility, LOD and LOQ values) are also conducted for the developed method. Ten samples supplied from different suppliers in different countries were tested and flavonoid contents were determined.

RESULTS:

Total flavonoid contents of the samples were found between 1.1742% ± 0.0039 and 2.0058% ± 0.0030. LOD and LOQ values were calculated as 0.2804 x 10-3 and 0.9346 x 10-3 respectively.

CONCLUSIONS:

In current study, we developed an HPLC method, which is more sensitive and accurate, for the determination of total flavonoid content expressed as rutoside.

REFERENCES:

1. Baytop T (1999). In: Türkiye'de Bitkilerle Tedavi. Geçmişte ve Bugün. 2nd Edition. Nobel Tıp Kitabevleri, İstanbul, pp 251.
2. Hellinger R et al. (2014). Journal of Ethnopharmacology, 151: 299-306.
3. Ergene Öz B, Saltan İşcan G (2017). In: Demirezer Ö, Saraçoğlu İ, Şener B, Köroğlu A, Yalçın FN (ed). FFD Monografları Bitkiler ve Etkileri. 3rd Edition. Akademisyen Kitabevi, Ankara, pp 1107.

P-045: ISOLATION AND QUANTIFICATION OF FLAVONOIDS FROM ZOSIMA ABSINTHIFOLIA

[1] Yaylaci, B., [1] Bahadir Acikara, O., [1] Kurtul, E.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

Zosima absinthifolia (Vent.) Link (Apiaceae), grows naturally in Turkey as the only species of this genus (1), and its medicinal usage has been recorded; fruits are used as digestive, carminative and anti-inflammatory agent. Aerial parts of the plant are used to relieve cough, indigestion and bowel disorders in Turkey, as well as in Iran and Pakistan (2,3). The aim of this study is isolation and quantitation of the flavonoids from Z. absinthifolia aerial parts.

MATERIALS AND METHODS:

Aerial parts of the plant was extracted with n-hexane, ethylacetate and methanol respectively by stirring at 50 ºC. The methanol extract of the Z. absinthifolia (22.3278 g) was subjected to column chromatography on silicagel to obtain 90 fraction by eluting chloroform:methanol:water (65:25:4) mixture. Fraction 10-12 (259,9 mg) were purified on preparative thin layer chromatography (RP-18, Merck 5559) using chloroform:methanol: H2O (40:15:2) solvent system. Fraction 18-19 was separated by semi-preparative HPLC. Structures of the isolated compounds were elucidated on the basis of their MS and NMR data as well as chemical correlations with known compounds described in the literature.

To prepare calibration curve, peak area of isorhamnetin-3-O-rutinoside-7-O-glucoside solution was plotted against the concentration. The compound was prepared at seven different concentration levels (0.9, 0.45, 0.225, 0.1125, 0.09, 0.045, 0.0225 mg/ml). Methanolic extract of plant was obtained using condenser during 3 hours. Triplicate injections of 10 µl for each solution were performed.

RESULTS:

Isorhamnetin-3-O-rutinoside (44 mg) and isorhamnetin-3-O-rutinoside-7-O-glucoside (27 mg) were obtained as flavonoids. Quantition of the compounds was also performed by HPLC. Percentage of isorhamnetin-3-O-rutinoside-7-O-glucoside and isorhamnetin-3-O-rutinoside was determined as 0,33±0.04 g/100 g and 0,50±0.08 g/100 g plant material, respectively.

CONCLUSIONS:

Aerial parts of Z. absinthifolia, isorhamnetin-3-O-rutinoside and isorhamnetin-3-O-rutinoside-7-O-glucoside have been isolated for the first time.

REFERENCES:

1. Davis PH (1972). Flora of Turkey and the East Aegean Islands Vol 4. Edinburgh University Press. Edinburgh.
2. Razavi SM, Ghasemiyan A, Salehi S, Zahri F (2009). Eurasian Journal of BioSciences, 4: 25-28.
3. Goodman SM, Ghafoor A (1992). Fieldiana Botany, 31: 1-84.

P-046: GAS-CHROMATOGRAPHIC PROFILING OF PHYSOSPERMUM CORNUBIENSE (L.) DC. ESSENTIAL OIL

[1] Ozek, G., [1] Berdanoglu, C.A., [2] Celik, M., [3] Cetin, O., [4] Baser, K.H.C.

[1]Anadolu University, Faculty of Pharmacy, Department of Pharmacognosy, Eskisehir, Turkey

[2]Selcuk University, Advanced Technology Research and Application Center, Konya, Turkey

[3]Selcuk University, Science Faculty, Deparment of Biotechnology, Konya, Turkey

4Near East University, Faculty of Pharmacy, Department of Pharmacognosy, Lefkoşa (Nicosia) TRNC, Mersin, Turkey

INTRODUCTION:

Physospermum cornubiense (L.) DC., belongs to the Apiaceae family and is the only representative of the genus Physosperm in Turkey (1). In Turkey, the species is found in Bolu, Karabük, Artvin, Bursa, Erzincan, Gümüşhane, Hatay, İçel, Konya provinces. General distribution of the species includes Southern and Western Europe, Cyprus, Crimea, Southern Russia, Caucasus, North West Iran (2). In literature, there are reports about essential oils of the species growing in Iran and Balkans (3, 4).

MATERIALS AND METHODS:

The plant was collected during flowering in Hatay (Belen) province of Turkey. The dried plant material was subjected to hydrodistillation in Clevenger type apparatus to yield essential oil. The chemical composition was investigated with GC-FID and GC/MS techniques (5).

RESULTS:

The main constituents of the essential oil were presented by the sesquiterpene hydrocarbons, β-bisabolene (23.8%), germacrene D (4.3%), β-caryophyllene (3.2%) and (Z)-β-farnesene (3.3%). The second major group, the oxygenated sesquiterpenes were presented by caryophyllene oxide (6.6%) and 1,5-epoxy-salvial-4(14)-ene (2.5%). The oil contained high amount of fatty acids like hexadecanoic acid (14.5%) and tetradecanoic acid (3.7%).

CONCLUSIONS:

The present work is the first study on essential oil of Physospermum cornubiense growing in Turkey. The oil was found to be reach with sesquiterpenes.

REFERENCES:

1. http://tubives.com/index.php?sayfa=1&tax_id=4225
2. Davis PH (1972). Flora of Turkey and the East Aegean Islands, Vol. 4, Edinburg University Press, Edinburg.
3. Khalilzadeh M, Tajbakhsh M, Glohami F, Hosaseinzadeh M, Dastoorani P, Norouzi M, Dabiri H (2007). J. Essent. Oil Res, 19(6): 567-568.
4. Kapetanos C, Karioti A, Bojović S, Marin P, Veljić M, Skaltsa H (2008). Biochem. & Biodivers., 5(1): 101-119.
5. Ozek G, Tekin M, Haliloglu Y, Baser KHC, Ozek T (2018). Rec. Nat. Prod, 12(2): 142-159.

P-047: SIMULTANEOUS ANALYSIS OF LYCORINE AND GALANTHAMINE IN NARCISSUS TAZETTA L. SUBSP. TAZETTA L. BY HPLC-PDA

[1] Karakoyun, C., [1] Onur, MA., [1] Unver Somer, N.

[1] Ege University, Faculty of Pharmacy, Department of Pharmacognosy, Izmir, Turkey

INTRODUCTION:

Lycorine is the prototype Amaryllidaceae alkaloid which is extensively studied for its various biological activities including anti-tumor, antiviral, antibacterial and anti-inflammatory activities(1). Galanthamine is the main medicinal Amaryllidaceae alkaloid having application against Alzheimer's Disease(2). Therefore, it is considered to be important to quantify these alkaloids in Amaryllidaceae species. In the present study, quantitative determination of lycorine and galanthamine, in bulbs and aerial parts of Narcissus tazetta L. subsp. tazetta L., collected from Western Turkey, were carried out.

MATERIALS AND METHODS:

A reverse phase HPLC method entegrated with Thermo Scientific PDA dedector was used. For the

chromatographic separation, Hichrom C-18 column (5µm, 250mm, 4.6mm) and an isocratic mobile phase of TFA-water-ACN (0.01:90:10) at a flow rate of 1.0 mL/min were utilized.

RESULTS:

The contents of lycorine and galanhamine in the bulbs and aerial parts was given in Table 1.

Table 1: Lycorine and Galanthamine Content of *N. tazetta* subsp. *tazetta*

Sample	Lycorine %	SD	Galanthamine %	SD
Bulbs	0,02498	0.00080	0,00514	0,00013
Aerial Parts	0,06723	0,00033	0,00548	0,00040

CONCLUSIONS:

Previously, the content of lycorine in the bulbs of Narcissus tazetta subsp. tazetta specimen, collected from Antalya has been reported(3). However to the best of our knowledge this is the first report on the quantification of galanthamine in N. tazetta subsp. tazetta of Turkish origin.

ACKNOWLEDGEMENTS

HPLC analysis is carried out in Ege University, Faculty of Pharmacy, Pharmaceutical Sciences Research Laboratory (FABAL).

REFERENCES:

1. Bastida J, Lavilla R, Viladomat F (2006). Alkaloids: Chemistry and Biology, 63:87-179.
2. Ago Y, Koda K, Takuma K, Matsuda T (2011). Journal of Pharmacological Sciences, 116(1):6-17.
3. Muhtar F, Şener B, editors. (1996) In:Evaluation of Amaryllidaceae Plants Exported From Turkey Regarding Lycorine XIth symposium on plant originated crude drugs, Ankara University Press; 1997.

P-048: PHYTOCHEMICAL STUDIES ON NARCISSUS TAZETTA L. SUBSP. TAZETTA L.

[1] Karakoyun, C., [1] Onur, MA., [2] Masi, M., [2] Cimmino, A., [2] Evidente, A., [1] Unver Somer, N.

[1]Ege University, Faculty of Pharmacy, Department of Pharmacognosy, Izmir, Turkey

[2]University of Naples Federico II, Department of Chemical Sciences, Naples, Italy

INTRODUCTION:

The genus Narcissus L. belongs to the family Amaryllidaceae, a monocotyledonous family represented by about 1100 species in 85 genera(1). Amaryllidaceae plants reproduce alkaloids with a wide range of biological activities(2). Narcissus tazetta L. subsp. tazetta L. is a widely distributed bulbous plant known for its biologically active Amaryllidaceae alkaloids(2, 3). In this study, chemical characterization of alkaloids, isolated from the bulbs of this Amarillydaceae species collected from Muğla/ Turkey, will be described.

MATERIALS AND METHODS:

The extraction of plant material was achieved using the classical acid-base extraction procedure for alkaloids(4). Column chromatography and preparative chromatography were used to isolate and purify alkaloids. The structures of the compounds were determined by using advanced spectroscopic techniques (1D, 2D NMR, MS).

RESULTS:

Phytochemical studies on N. tazetta subsp. tazetta, resulted in the isolation of 4 Amaryllidaceae alkaloids including lycorine, pseudolycorine, 11-hydroxygalanthine, and galanthamine. The isolated compounds excluding galanthamine belong to lycorine subgroup of Amaryllidaceae alkaloids. Galanthamine is an Amaryllidaceae alkaloid with acetylcholinesterase inhibitory activity used in the treatment of mild to moderate Alzheimer's Disease(2, 3).

CONCLUSIONS:

Previously, a limited number of alkaloids including lycorine have been isolated from a different specimen of N. tazetta subsp. tazetta collected from South Turkey(5). However, to the best of our knowledge, this is the first report of pseudolycorine, 11-hydroxygalanthine and galanthamine from this Amaryllidaceae species.

ACKNOWLEDGEMENTS:

This study was realized within the framework of Erasmus Plus Programme.

REFERENCES:

1. J W. Amaryllidaceae. In: A S, editor. A dictionary of the flowering plants&ferns. 8th ed. Cambridge Cambridge University Press; 1988. p. 49-50.
2. Cimmino A, Masi M, Evidente M, Superchi S, Evidente A (2007). Chirality, 29(9):486-99.
3. Jaume B, Rodolfo L, Francesc V (2006). The Alkaloids: Chemistry and Biology, 63:87-179.
4. Cordell GA (1981) In: Introduction to alkaloids. New York: John Wiley & Sons Inc.
5. Orhan I, Sener B (2003). Chemistry of Natural Compounds, 39(4):383-6.

P-049: ANTIMICROBIAL ACTIVITY AND CHEMICAL COMPOSITION OF ESSENTIAL OILS FROM AERIAL PARTS AND RADIX OF HYPERICUM HİRCİNUM L. SUBSP. MAJUS (AİTON) N. ROBSON

[1] Kirci D., [2] Kose YB.,[1] Demirci B.

[1] Anadolu University, Faculty of Pharmacy, Department of Pharmacognosy, Eskişehir, Turkey

[2] Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Eskişehir, Turkey,

INTRODUCTION:

Plant species of the genus *Hypericum (*Hypericaceae) are well known for their use in traditional medicine as healing sore throats, colds, and an antitussive, due to the therapeutic effects of its many different species (1,2). One of them is Hypericum hircinum L. subsp. majus ***(Aiton) N. Robson*** which thrives in Turkey, S. Europe, Cyprus, and Syria, a semi-evergreen shrub with sessile, opposite and ovate-lanceolate-shaped leaves with translucent glands(3). In this present work, chemical composition of essential oils from aerial parts and radix of H. hircinum subsp. majus and their antibacterial and antifungal properties were evaluated.

MATERIALS AND METHODS:

The radix and aerial parts of H. hircunum subsp. majus were collected in July 2017 from Kirazlı Waterfall, Eskisehir (Turkey). The essential oils (EOs) were obtained by hydrodistillation using a Clevenger type apparatus for 3h. EOs were analyzed both by GC-FID and GC-MS, simultaneously. EO of H. hircunum aerial parts was examined for antimicrobial activity by the microdilution broth susceptibility assay against Staphyloccoccus aureus, Streptococcus pynogenes, Escherichia coli and Candida albicans.

RESULTS:

Germacrene D (26.4%), α-pinene (8.5%), ð-cadinene (5.5%), γ-muurolene (4.0%), 3-methyl nonane (2.8%), (Z)-β-farnesene (2.8%), γ-cadinene (2.5%) and α-cadinol (2.4%) were found as main constituents of the aerial parts of H. hircinum EO. The EO of H. hircinum radix were characterized with undecane (38.9%), α-pinene (14.2%), 3-methyl nonane (9.2%), 2-methyl-decane (5.8%) and α-cadinol (2.1%). The antimicrobial activity (Minimum Inhibitory Concentration (MIC)) against S. pyogenes ATCC 13615 (219 µg/mL), E. coli NRRL B-3008 (8.75 mg/mL), S. aureus ATCC 6538 (109 µg/mL) and C. albicans ATCC 90028 (55 µg/mL) were observed by EO of H. hircinum aerial parts, respectively.

CONCLUSION:

Among the tested microorganism, S. aureus and C. albicans were found to be more sensitive to the EO of H. hircinum aerial parts. The EO was founds as effective against skin pathogens.

REFERENCES:

1. Barnes, J, Anderson, LA, Phillipson, JD (2001). Journal of Pharmacy and Pharmacology, 53(5):583-600.
2. Pieroni A, Quave CL, Santoro RF (2004). Journal of Ethnopharmacology. 95(2-3):373-384.
3. Davis, P. H. 1965. In: Flora of Turkey. Vol. 2. Edinburgh: University of Edinburgh Press. 140, pp:366.

P-050: ESSENTIAL OIL COMPOSITION OF ROOTS, AERIAL PARTS AND FRUITS OF FERULAGO MACROSCIADIA BOISS. ET BAL.

[1] Demirci, B., [1] Kirci, D., [2] Kilic, C. S., [3] Gurbuz, I., [4] Duman, H.

[1] Anadolu University, Faculty of Pharmacy, Department of Pharmacognosy, Eskişehir, Turkey

[2] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

[3] Gazi University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

[4] Gazi University, Faculty of Science, Department of Biology, Ankara, Turkey

INTRODUCTION:

Ferulago W. Koch is a genus of the family Apiaceae having important medicinal properties. This genus is known with the name “Çakşır” in Turkey and 35 taxa of the genus grow naturally in our country. [1, 2]. Members of this genus are used in traditional medicine for their various biological activities (e.g. sedative, digestive, carminative, tonic), however they are mostly known for their aphrodisiac activities [3]. In this study we examined the composition of the essential oil of the roots, aerial parts and fruits of Ferulago macrosciadia which is an endemic species for Turkey.

MATERIALS AND METHODS:

Essential oils of the grounded roots, aerial parts and fruits were obtained by hydrodistillation using a Clevenger type apparatus for 3h. Essential oils were analyzed both by GC-FID and GC-MS, simultaneously.

RESULTS:

The main components of the plant organs are given in the following table.

Table 1. Essential oil compositions of different parts of F. macrosciadia

Plant organ	Main components	%
Roots	2,5-Dimethoxy-p-cymene	58.6
	Carvacrol methyl ether	15.5
	p-Cymene	8.8
	Terpinolene	6.9
	γ-Terpinene	4.1
Aerial parts	2,5-Dimethoxy-p-cymene	26.5
	Nonacosane	9.3
	Limonene	9.3
	Hexadecanoic acid	7.6
	Terpinolene	7.2
Fruits	Limonene	34.1
	α-Pinene	9.2
	p-Cymene	10.8
	γ-Terpinene	23.6
	Terpinolene	5.7

CONCLUSIONS:

The obtained results are compatible with the essential oil profiles of different parts of various Ferulago species found in the literature.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-115S364)

REFERENCES:

1. Davis PH (Ed.) (1972) In: Flora of Turkey and the East Aegean Islands, University Press, Edinburgh, Vol 4, pp 462-464.
2. Troia A, Raimondo FM, Castellano G, Spadaro V (2012). Plant Biosystems, 146: 330-337.
3. Selçuk SS, Özsoy N, Özbek Çelik B, Akalın Uruşak E (2017), İstanbul Journal of Pharmacy, 47(3): 101-106.

P-051: ANTIOXIDANT, ANTI-UREASE AND ANTICHOLINESTERASE ACTIVITIES OF ALCEA DISSECTA

[1] Kahvecioglu, D., [1] Taskin, T., [2] Sahin, T., [3] Dogan, A.

[1] Marmara University, Faculty of Pharmacy, Department of Pharmacognosy, Istanbul, Turkey

[2] Marmara University, Faculty of Pharmacy, Department of Biochemistry, Istanbul, Turkey

[3] Marmara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Istanbul, Turkey

INTRODUCTION:

Alcea L. is taxonomically assigned to Malvaceae subfam. Malvoideae, tribe Malveae. Alcea is represented worldwide by about 70 species. Alcea shows the highest counts of species in Iran, Russia, and Turkey, in descending order (1). Alcea dissecta (Baker) Zoh. is known as Govik in Turkey. The leaves of plant is used for injuries and asthma (2). To our knowledge, there are no published reports on biological activity of different extracts from Alcea dissecta aerial parts. Therefore, the purpose of this study was to evaluate in vitro antioxidant, anti-urease and anticholinesterase activities of different extracts from plant.

MATERIALS AND METHODS:

The petroleum ether, chloroform, ethanol and ethanol: water (1:1, v/v) extracts were obtained using the Soxhlet and maceration methods. The antioxidant activities of these different extracts from plant were examined using DPPH, TEAC, FRAP and CUPRAC methods, including total phenolic contents (3). In addition, the anti-urease and anticholinesterase activities of different extracts were investigated using indophenol and Ellman methods, respectively (4, 5).

RESULTS:

In this study, ethanol: water (1:1, v/v) extracts obtained from Soxhlet (IC50:0.091 mg/mL) and maceration (IC50:0.1 mg/mL methods exhibited the strongest DPPH radical scavenging activity. Soxhlet chloroform extract had higher FRAP (0.470 mM Fe2+/mg extract) and CUPRAC (0.092 mM trolox/mg extract) values other extracts. In addition, maceration ethanol extract showed stronger anti-urease (38.59%) and anticholinesterase (94.66%) activity than other extracts.

CONCLUSIONS:

In this study, it was revealed that maceration and Soxhlet methods were the most suitable technical for anti-urease, anticholinesterase and antioxidant activity, respectively.

REFERENCES:

1. Erkan et al., (2012). Turk J Bot, 36:603-636.
2. Altundag et al., (2011). Procedia Social and Behavioral Sciences, 19:756–777.
3. Taşkın D et al., (2017). Chiang Mai Journal of Science 44:1-12.
4. Ghous et al., (2010). BLM, 2(4):64-69.
5. Ellman et al., (1961). Biochem Pharmacol, 7:88-95.

P-052: THE INVESTIGATION OF BIOLOGICAL ACTIVITIES OF PLANTAGO LANCEOLATE AERIAL PARTS AND ROOTS

[1] Taskin, T., [2] Sahin, T., [1] Kahvecioglu, D., [3] Senkardes, İ.

[1] Marmara University, Faculty of Pharmacy, Department of Pharmacognosy, Istanbul, Turkey

[2] Marmara University, Faculty of Pharmacy, Department of Biochemistry, Istanbul, Turkey

[3] Marmara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Istanbul, Turkey

INTRODUCTION:

Plantago lanceolata L. is a species of the genus Plantago in the Plantaginaceae botanical family. Abundant throughout Europe, North- and Central Asia. There are reports of the use of Plantago lanceolata in folk medicine: In Turkey, fresh leaves of P. lanceolata are used eaten. In Guatemala, the herbal substance is administered in conjunctivitis/eye irritation and for the treatment of wounds, ulcers, bruises and sores. In North-West Greece, infusions of Plantago lanceolata leaves are used for curing stomach spasms. It has been determined that the plant has anti-inflammatory, anti-antioxidant, antibacterial, antiviral, immunostimulant and spasmolytic effects (1,2). The extraction procedures and solvents are an important step in processing bioactive constituents from the plant materials. For this reason, it is essential to examine in detail the effect of extraction methods and solvents on the biological activities of plants. The best of our knowledge, there are not any study on anti-urease and anticholinesterase activities of this species. Therefore, the aim of this study was to evaluate in vitro antioxidant, anti-urease and anticholinesterase activities of different extracts from P. lanceolate aerial parts and roots.

MATERIALS AND METHODS:

The petroleum ether, chloroform, ethanol and ethanol: water (1:1, v/v) extracts were obtained using the Soxhlet and maceration methods to root and aerial parts of the plant. The antioxidant activities of these different extracts from plant were examined using DPPH, TEAC, FRAP and CUPRAC methods, including total phenolic contents (3). In addition, the anti-urease and anticholinesterase activities of different extracts were investigated using indophenol and Ellman methods, respectively (4,5).

RESULTS:

According to the results of the study, it was observed that the Soxhlet ethanol: water (1:1, v/v) extracts extracts obtained from roots (69.41%) and aerial parts (77.27%) showed stronger free radical scavenging activity than other extracts. It was determined that the maceration chloroform extract obtained from roots (23.18%) and Soxhlet chloroform extract obtained from aerial parts (33.58%) had stronger anti-urease activity than the other extracts. In addition, Soxhlet ethanol extract obtained from roots (74.97%) and Soxhlet chloroform extract obtained from aerial parts (77.87%) exhibited the strongest anticholinesterase activity.

REFERENCES:

1. Konczak I, Dalar A., (2014). Nova Biomedical, New York. pp 201-206.
2. HMPC (2011). Europeam Medicines Agency. pp 3-24.
3. Taşkın D et al., (2017). Chiang Mai Journal of Science 44:1-12.
4. Ghous et al., (2010). BLM, 2(4): 64-69.
5. Ellman et al., (1961). Biochem Pharmacol, 7;88-95.

P-053: IN VITRO BIOLOGICAL ACTIVITIES OF DIFFERENT EXTRACTS FROM RUSCUS ACULEATUS L.

[1] Guler, E., [1] Taskin, T., [2] Sahin, T., [3] Bulut, G.

[1] Marmara University, Faculty of Pharmacy, Department of Pharmacognosy, Istanbul, Turkey

[2] Marmara University, Faculty of Pharmacy, Department of Biochemistry, Istanbul, Turkey

[3] Marmara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Istanbul, Turkey

INTRODUCTION:

Ruscus aculeatus L. (butcher's broom) belonging to the Liliaceae family, is a small evergreen shrub widespread in western, southern and south-central Europe (1). Preparations from an alcoholic extract of its rhizome have been used for the treatment of veinous insufficiency, haemorrhoids, and capillary fragility. Recently, sulfated steroidal derivatives, triterpenes, and sterols were isolated from the rhizome of R. aculeatus (2). The extraction procedures and solvents are an important step in processing bioactive constituents from the plant materials. For this reason, it is essential to examine in detail the effect of extraction methods and solvents on the biological activities of plants. Therefore, the aim of this study was to evaluate in vitro antioxidant, anti-urease and anticholinesterase activities of different extracts from Ruscus aculeatus rhizome.

MATERIALS AND METHODS:

The petroleum ether, chloroform, ethanol and ethanol:water (1:1, v/v) extracts were obtained using the Soxhlet and maceration methods. The antioxidant activities of these different extracts from plant were examined using DPPH, TEAC, FRAP and CUPRAC methods, including total phenolic contents (3). In

addition, the anti-urease and anticholinesterase activities of different extracts were investigated using indophenol and Ellman methods, respectively (4,5).

RESULTS:

According to the results obtained from this study, Soxhlet ethanol (92.56%, 1 mg/mL) and maceration ethanol (91.90%, 1mg/mL) extracts showed stronger ABTS radical scavenging activity than the other extracts. In addition, Soxhlet chloroform extract exhibited the strongest CUPRAC (0.86±0.001 mM trolox/mg extract) and DPPH (IC50: 0.17± 0.004 mg/mL) antioxidant activity. It was also found that the maceration ethanol (34.24%) and ethanol: water (1:1, v/v) (35.15%) extracts exhibited the strongest anti-urease activity. Soxhlet chloroform (94.37%) and ethanol: water (1:1, v/v) (92.68 %) extracts showed higher anticholinesterase activity than other extracts.

CONCLUSIONS:

According as a results, the ethanol and ethanol: water (1:1, v/v) extracts prepared using Soxhlet and maceration method and Soxhlet chloroform extract was found to exhibited stronger biological activity than the other extracts.

REFERENCES:

1. Moyano et al., (2006). Biologia Plantarum, 50 (3):441-443.
2. Mimaki et al., (1998). Chem. Pharm. Bull, 46(2):298-303.
3. Taşkın D et al., (2017). Chiang Mai Journal of Science 44:1-12.
4. Ghous et al., (2010). BLM, 2(4): 64-69.
5. Ellman et al., (1961). Biochem Pharmacol, 7:88-95.

P-054: INVESTIGATION OF ANTICHOLINESTERASE ACTIVITIES OF DIFFERENT PARTS OF RHEUM RIBES

[1] Sahin, T., [2] Taskin, T., [2] Guler, E.

[1]Marmara University, Faculty of Pharmacy, Department of Biochemistry, Istanbul, Turkey

[2]Marmara University, Faculty of Pharmacy, Department of Pharmacognosy, Istanbul, Turkey

INTRODUCTION:

Rheum ribes is one of the wild rhubarb species belonging to Polygonaceae family and utilized as vegetable in various countries. It is a perennial vegetable species spread from North and Central Asia to the other continents. It has also wild forms in Iran and Anatolia (1). Roots of the plant are used to treat diabetes, hemorrhoids, ulcer, diarrhea and expectorant activity has been reported (2). Also, it has some medicinal properties such as preventing of stomach upset, vomiting, measles and smallpox and increasing appetite (3). In the literature reviews, it was observed that there is not any study on anticholinesterase activity of plant different parts. Therefore, the aim of this study was to evaluate in vitro anticholinesterase activities of methanol extracts from different parts of Rheum ribes.

MATERIALS AND METHODS:

The methanol extracts of different parts (flower, radix, leaves, and young shoots) of the plant were prepared using the Soxhlet, maceration and ultrasonic bath extraction methods. The anticholinesterase activities of these different extracts were examined using Ellman method (4).

RESULTS:

According to the results the radix (45.97%), flowers (71.90%) and leaves (64.90%) methanol extracts obtained from ultrasonic bath method and young shoots extract (87.98%) obtained by Soxhlet extraction method exhibited stronger anticholinesterase activity than the other extracts.

REFERENCES:

1. Polat et al., (2015). Indian Journal of Traditional Knowledge, 1:69-75.
2. Sındhu et al., (2010). International Journal of Pharmacy and Pharmaceutical Sciences, 2:90-92.
3. Shafaghat et al., (2014). Journal of Pharmaceutical and Health Sciences, 2:115-123.
4. Ellman et al., (1961). Biochemical Pharmacology, 7:8-95.

P-055: FLAVONOIDS FROM THE ETHYLACETATE EXTRACT OF SCORZONERA CANA VAR JACQUINIANA AERIAL PARTS

Kurtul, E., Bahadir Acikara, O.

Ankara University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

S. cana (C.A. Meyer) Hoffm. var. jacquiniana (W. Koch) Chamb., from Asteraceae family grows naturally in Europe, Anatolia, Syria, Iraq, Caucasia and Iran (1). In Turkish folk medicine this plant is known as “karakök or tekesakalı” (2). The aim of the current study is to investigate phytochemical content of the aerial parts ethyl acetate extract.

MATERIALS AND METHODS:

Dried and powdered aerial parts of the plant material were macerated in methanol at room temperature. Afterwards, the extract was filtered and evaporated until dryness under reduced pressure at 50°C. The crude extract was subjected to liquid partitioning yielding the fractions of petroleum ether, chloroform, ethyl acetate and water. Separation was carried

out from ethyl acetate extract on silica gel column chromatography by eluting with ethyl acetate: methanol: water (100:13,5:10) mixture. Further purifications from the fractions obtained from the ethyl acetate extract were performed by preparative thin layer chromatography to obtain flavonoids. Structure of the compounds were elucidated by using spectroscopic techniques (1H,13C and 2D-NMR, MS).

RESULTS:

Chromatographic separation of the ethyl acetate extract yielded apigenin-7-O-glucoside (1), apigenin-7-O-rutinoside (2), luteolin-7-O-glucoside (3), isovitexin (4), orientin (5) and isoorientin (6)

CONCLUSIONS:

In current study S. cana var. jacquiniana aerial parts have been investigated for its flavonoid content for the first time.

REFERENCES:

1. Davis PH (1975). Flora of Turkey and the East Aegean Islands, vol. 5. University Press, Edinburgh, pp 632–657.
2. Turan M, Kordali S, Zengin H, Dursun A, Sezen Y (2003). Soil and Plant Sciences, 53: 129-137.

P-056: NEUROPROTECTIVE EFFECTS OF SOME FRITILLARIA L. SPECIES GROWING IN EAST ANATOLIA

[1] Yaris, E., [2] Kilic, M., [3] Aslay, M., [4] Kaya, E., [2] Sener, B.

[1] Dicle University, Faculty of Pharmacy, Department of Pharmacognosy, Diyarbakır, Turkey

[2] Gazi University, Faculty of Pharmacy, Department of.Pharmacognosy, Ankara, Turkey

[3] Erzincan Horticultural Research Institution, Ornamental Plant Breeding and Agronomy Section, Erzincan, Turkey

4Department of Ornamental Plant Breeding and Agronomy, Atatürk Horticultural Central Research Institute, Yalova, Turkey

INTRODUCTION:

Medicinal plants represent an important source of bioactive compounds that could be used for new drugs development. Most of the bulbous plants are known for their medicinal purposes in addition to their ornamental value. Turkey is one of the home countries of many beautiful bulbous plants (1). The ornamental bulbous plant member of the genus Fritillaria L. has a wide range of medicinal activities known and it is known as Bei-Mu in the Traditional Chinese Medicine. It is widely distributed in Asia and traditionally used for treatment of different human diseases, especially mental illnesses. In continuation of our extensive studies on finding new natural inhibitors from Turkish bulbous plants, we have now aimed to screen the AChE and BChE inhibitory activity of extracts prepared from 19 Fritillaria species (Liliaceae) collected from East Anatolia that were not well studied with respect to their neuroprotective potentials.

MATERIALS AND METHODS:

19 Fritillaria L. were collected from different localities of the East Anatolia and the extracts of the bulbs were tested for their cholinesterase inhibitory activities using Ellman's spectrophotometric method adapted to ELISA microtiter assay.

RESULTS:

Our results indicated that the bulb extracts of Fritillaria species growing in East Anatolia exerted high to moderate BChE inhibition between 71.33±0.36 and 87.50±2.08 (galanthamine 72.76±0.82) at 200 mg/mL with no AChE inhibition. The highest value belonged to the methanolic extract of F. persica. These findings support the traditional use of Fritillaria species in the treatment of neurodegenerative disorders such as Alzheimer's Disease.

CONCLUSIONS:

It can be recommended that future studies should aim to determine the best method for large-scale cultivation of the active Fritillaria species and to detect the neuroprotective phytochemicals to establish the molecular mechanisms of neuroprotective effects of Fritillaria species.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (KAMAG-110G007)

REFERENCES:

1. Kaya, E.(ed.), (2014). In: Geophytes of Turkey, Vol. 1-3, Atatürk Central Horticultural Research Institute, Edition No: 96, Yalova.

P-057: EVALUATION OF ENZYME INHIBITORY ACTIVITY OF ETAHOLIC EXTRACTS OF THE ROOTS OF TWO FERULAGO SPP.

[1] Demirci, F., [1] Karaca, N., [2] Kilic, C.S., [3] Duman, H, [4] Gurbuz, I.

[1]Anadolu University, Faculty of Pharmacy, Department of Pharmacognosy, Eskisehir, Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

[3]Gazi University, Faculty of Science, Department of Biology, Ankara, Turkey

4Gazi University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

Inflammation is a biological response of cells and tissues for the stimuli of pathogens or injuries where cyclooxygenases (COX) and 5-lipoxygenases (5-LOX) may produce biologically active lipid molecules called eicosanoids. Plant extracts as well as natural and synthetic coumarins are known to inhibit such inflammations (1-3). As Ferulago angulata (Schlecht.) Boiss. was reported with anti-inflammatory activity as well (4), it was aimed in the present work to evaluate the 5-LOX and COX inhibitory activities of F. cassia Boiss. and F. isaurica Peşmen from Turkey.

MATERIALS AND METHODS:

In vitro enzyme inhibitory activities were performed on the ethanol extracts of the dried underground parts of the Ferulago spp. spectrophotometrically on a 96-well format. Nordihydroguaiatic acid (NDGA) was used as a positive control.

RESULTS:

LOX and COX inhibitory activity results can be seen in Table 1.

Table 1. Percentage (%) 5- LOX and COX inhibition results of the extracts

Samples	LOX *	COX *
F. cassia	31.3	4.6
F. isaurica	10.9	5.3
NDGA (Standard)**	5.1	100

**LOX and COX activities were performed on 50 µg/mL and 125 µg/mL extracts, respectively*

***NDGA concentration was 1 µg/mL for LOX and 125 µg/mL for COX.*

CONCLUSIONS:

Both Ferulago species showed 5-LOX inhibitory effect, however their COX inhibitory activities were weak compared to the standard. Nevertheless, it can be concluded that the evaluated Ferulago species may be further elaborated for anti-inflammatory activity.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-115S364).

REFERENCES:

1. De Cássia da Silveira e Sá R, Andrade LN, dos Reis Barreto de Oliveira R, de Sousa DP (2014). Molecules, 19(2): 1459.
2. Yauan G, Wahlqvist M, He G, Yang M, Li D (2006). Asia Pacific Journal of Clinical Nutrition, 15(2): 143.
3. Fylaktakidou KC, Hadjipavlou Litina DJ, Litinas KE, Nicolaides DN (2004). Current Pharmaceutical Design, 10 (30): 3813.
4. Rafieian kopaei M, Shahinfard N, Rouhi Boroujeni H, Gharipour M, Darvishzadeh Boroujeni P (2014). Evidence Based Complementary Alternative Medicine, Article ID 680856.

P-058: ACETHYLCHOLINE AND BUTYRYLCHOLINE ESTERASE INHIBITORY ACTIVITY OF PRANGOS TURCICA FRUITS

[1] Erucar, F.M, [2] Ozden Yilmaz, T., [1] Yazici Tütünis, S., [3] Akalin Urusak, E. [1] Tan, N., [1] Miski, M.

[1] Istanbul University, Faculty of Pharmacy, Department of Pharmacognosy, Istanbul, Turkey

[2]Istanbul University, Faculty of Pharmacy, Department of Biochemistry, Istanbul, Turkey

[3] Istanbul University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Istanbul, Turkey

INTRODUCTION:

Alzheimer's disease is one of the most common variety of dementia illnesses with a rate of 60-70%. Currently 50 million patients have this disease and the number of Alzheimer patients has been increased by approximately 10 million every year. Due to the magnitude of such epidemic amongst the elder population, World Health Organization (WHO) has defined dementia as a priority issue of public health (1). In this project, the traditional uses of the Prangos genus and related genera of Apiaceae family such as Ferula, Ferulago and Angelica among the people were investigated in terms of coumarin derivatives and terpenic compounds. Due to the well documented cholinesterase inhibitor activities of coumarin derivatives (2), anti-Alzheimer activities were most likely associated with both plant extracts that mainly contain coumarin derivatives. Despite the limited number of studies performed on the anti-cholinesterase activities of natural coumarin derivatives isolated from Prangos species, these compounds may provide new leads for the anti-alzheimer drug development studies. Prangos turcica A. Duran, M. Sağıroğlu & H. Duman, an endemic species growing in the southern Turkey, has only been previously investigated for the essential oil composition of its fruits (3, 4).

MATERIALS AND METHODS:

In addition to the dichloromethane and methanol extracts, infusion and decoction of P. turcica fruits were prepared. Acetylcholine esterase (AChE) and butyrylcholine esterase (BChE) inhibitory activities have been determined according to the method developed by Ellman et al. in order to examine anti-Alzheimer activity of extracts (5).

RESULTS:

All the extracts of P. turcica fruits inhibited BChE activity in a dose dependent-manner and dichloromethane extract was found to be the most active extract (86.85% at 0.1 mg/mL concentration). However, the extracts showed only weak inhibitor activity against AChE.

CONCLUSIONS:

The results have revealed that these extracts which can be used for the alleviation of Alzheimer's disease symptoms, also they were suitable and promising for anti-Alzheimer drug development. Our bioactivity directed isolation studies are currently in progress.

REFERENCES:

1. World Health Organization. "Dementia, Fact sheet". WHO. 2017 http://www.who.int/mediacentre/factsheets/fs362/en/
2. Souza LG, Renno MN, Figueroa-Villar JD (2016). Chemico-Biological Interactions 254: 11-23.
3. Duran A, Sağıroğlu M, Duman H (2005). Annales Botanici Fennici, 42: 67-72.
4. Özek G, Özek T, Başer KHC, Duran A, Sağıroğlu M, Duman H (2006). Journal of Essential Oil Research, 18: 511-514.
5. Ellman GL, Courtney KD, Andres V, Featherstone RM (1961). Biochemical Pharmacology, 7: 88-95.

P-059: VOLATILE COMPONENTS OF THE N-HEXANE EXTRACT OF NEOMURETIA PISIDICA (KIT TAN) KLJUYKOV, DEGTJAREVA & ZAKHAROVA

[1,2] Karadag A.E.,[3] Demirci B., [4] Cecen O., [1] Tosun F.,

[1]Istanbul Medipol University, School of Pharmacy, Department of Pharmacognosy, Istanbul, Turkey

[2]Anadolu University, Graduate School of Health Sciences, Eskisehir, Turkey

[3]Anadolu University, School of Pharmacy, Department of Pharmacognosy, Eskisehir, Turkey

4Karamanoglu Mehmetbey University, Ermenek Vocational High School, Department of Plant and Animal Production, Medical and Aromatic Plants Programme, Karaman, Turkey.

INTRODUCTION:

Neomuretia H. Wolff (Apiaceae) is a small genus of geophytic herbs that currently includes two species and distributed in the southern Turkey, and northern Iraq (1). N. pisidica is an endemic species growing in the Karaman province of Turkey and used as a food by local villagers.

MATERIALS AND METHODS:

The air dried plant material was macerated initially with n-hexane. After filtration and evaporation the extract prepared for GC-FID and GC-MS analysis.

RESULTS:

Main components of aerial parts of n-hexane extract were characterized as 1,8-cineole (23.4%), camphor *(21.4%), 2-ethyl hexanol (14.6%), α-pinene (7.2%), and verbenone (6.4%), respectively. Methyl linoleate (19.3%), 1,8-cineole (16.5%), camphor (13.2%), α-pinene (6.1%) and 2-ethyl hexanol (4.9%) were found in the hexane extract of root. Whereas, 1,8-cineole (23.3%), camphor (20.3), 2-ethly hexanol (14.2%), α-pinene (9.9%), and limonene (4.1%) were the major components of the hexane extract of fruit.*

CONCLUSIONS:

When the volatile components of n-hexane extracts prepared from the three different parts of plant material were examined, they were found to contain similar chemical composition. While the root extract was rich in fatty acid esters, the other two extracts were rich in monoterpene compounds.

REFERENCES:

1. Zakharova EA, Kljuykov EV, Degtjareva GV, Samigullin T, Ukrainskaya UA, Downie SR (2016). Turkish Journal of Botany, 40(2):176-193.

P-060: DETERMINATION OF THE VOLATILE COMPOUNDS OF ANTHEMIS CRETICA SUBSP. ANATOLICA (BOISS.) GRIERSON

[1] Tosun F., [2] Kurkcuoglu M.

[1] Istanbul Medipol University, School of Pharmacy, Department of Pharmacognosy, Istanbul, Turkey

[2]Anadolu University, Faculty of Pharmacy, Department of Pharmacognosy, Eskisehir, Turkey

INTRODUCTION:

Genus Anthemis L. (Asteraceae) is represented by 50 species and Anthemis cretica by twelve subspecies in Turkey (1). In the current study essential oil of the aerial parts of A. cretica subsp. anatolica (Boiss.) Grierson was analyzed by GC-FID and GC-MS.

MATERIALS AND METHODS:

The air-dried plant material was hydrodistilled for 3 hours using a Clevenger-type apparatus, the resulting essential oil of A. cretica subsp. anatolica was analyzed by capillary GC and GC/MS using an Agilent GC-MSD system.

RESULTS:

Yield of essential oil obtained by hydrodistillation for A. cretica subsp. anatolica was found to be 0.22%. The essential oil of A. cretica subsp. anatolica was characterized by the presence of a high percentage of oxygenated sesquiterpenes (57.9%). Twenty-seven compounds were identified representing 96.6 % of the essential oil of A. cretica subsp. anatolica. The main components of the oil were spathulenol (27.0%) and hexadecanoic acid (14.3%). Hitherto the essential oil composition of A. cretica subsp. anatolica has not been investigated.

CONCLUSION:

Major components of the essential oil of A. cretica subsp. anatolica have been identified as spathulenol and hexadecanoic acid. Based on the previously published essential oil data (2-4), major components of A. cretica subsp. anatolica were quite distinct than those of A. cretica subsp. carpatica, subsp. columnae, subsp. messanensis as well as A. cretica subsp. pontica supporting the taxonomical separation of this subspecies from the aforementioned subspecies.

REFERENCES:

1. Grierson AJC, Yavin Z (1975) Anthemis L. In: Davis PH (ed). Flora of Turkey and the East Aegean Islands, vol. 5. Edinburgh University Press, Edinburgh, pp 174–221.
2. Riccobono L, Maggio A, Bruno M, Spadaro V and Raimondo FM (2017). Natural Product Research, (31)23: 2759-2767.
3. Pavlovic M, Lakusic D, Kovacevic N, Tzakou O and Couladis M (2010). Chemistry of Biodiversity, 7: 1231-1244.
4. Kilic O, Kocak A and Bagci E (2011) Z. Naturforsch, 66:535-540.

P-061: FROM NATURE TO NOVEL SOURCES OF PHYTO-PHARMACEUTICALS: AJUGA CHAMAEPITYS SUBSP. CHIA VAR. CHIA AND AJUGA BOMBYCINA

[1] Zengin, G. [2] Mahomoodally, F.M., [1] Aktumsek, A

[1] Selcuk University, Faculty of Science, Department of Biology, Konya, Turkey

[2] University of Mauritius, Department of Health Sciences, Réduit, Mauritius

INTRODUCTION:

Recent evidences suggest that plant-based extracts and metabolites exert a protective action on human health. The use of herbal medicines, phytonutrients and /or nutraceuticals are increasing exponentially throughout the world (1, 2). The present study was designed to evaluate biological activites (antioxidant and enzyme inhibitory potential) of Ajuga chamaepitys subsp. chia var. chia and A. bombycina.

MATERIALS AND METHODS:

The aerial parts of two Ajuga were collected in Konya, Turkey (during summer of 2016).The methanol, ethyl acetate, and water extracts were prepared from the Ajuga species. Antioxidant capacity was evaluated using different chemical assays (DPPH, ABTS, CUPRAC, FRAP, phosphomolybdenum, and metal chelating). Enzyme inhibitory properties were tested against cholinesterase, tyrosinase, α-amylase, and α-glucosidase enzymes.

RESULTS:

The water extract of A. chamaepitys exhibited the strongest antioxidant properties with a higher level of total phenolics (22.61 mgGAE/g extract). However, the ethyl acetate and methanol extracts showed greater enzyme inhibitory activity when compared to the water extracts.

CONCLUSION:

Current findings tend to suggest that both Ajuga species can be regarded as an important source of biologically-active compounds to design novel applications in food and pharmaceutical industry.

REFERENCES:

1. Ekor M (2014). Frontiers in Pharmacology 4:177.
2. Yirga et al., (2011). International Journal of Biodiversity and Conservation 3:709-714.

P-062: ESSENTIAL OIL OF MENTHA LONGIFOLIA VAR. CALLIANTHA: CHEMICAL COMPOSITION, ANTIOXIDANT, AND ENZYME INHBITORY PROPERTIES

[1] Bahadori, MB., [2] Zengin, G

[1] Maragheh University of Medical Sciences, Phytopharmacology Research Center, Maragheh, Iran

[2] Selcuk University, Faculty of Science, Department of Biology, Konya, Turkey

INTRODUCTION:

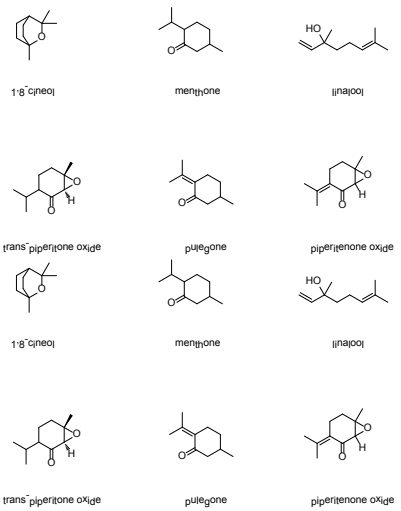
Mints are used as herbal tea, food additives, and traditional medicines all around the world (1). In this work, chemical composition of essential oil of wild mint (Mentha longifolia var. calliantha) was determined together with its antioxidant and enzyme inhibitory potential.

MATERIALS AND METHODS:

GC-MS analysis were used for identification of chemical composition of the essential oil. Six different methods were employed for examination of antioxidant ability including DPPH, ABTS, CUPRAC, FRAP, metal chelating, and Mo total antioxidant assays. Also, enzyme inhibitory analysis linked to Alzheimer's disease, diabetes mellitus, and skin disorders were performed (2).

RESULTS:

Results showed that 1,8-cineol (33.5%), linalool (15.1%), menthone (12.9%), and trans-piperitone oxide (12.6%) are the main volatile compounds of the essential oil. Moreover, the essential oil exhibited promising radical scavenging, reducing power, antidiabetic, anticholinesterase, and antityrosinase effects.



CONCLUSIONS:

Findings indicated that wild mint essential oil has valuable bioactive constituents and great potential for uses in food, pharmaceutical, and cosmeceutical industries.

ACKNOWLEDGEMENTS:

Authors would like to thank Mr. Shahram Bahadori for collection and Identification of plant material.

REFERENCES:

1. McKay DL, Blumberg JB (2006). Phytotherapy Research, 20:619-633.
2. Bahadori et al., (2017). Natural Product Communıcatıons, 12:1945-1948.

P-063: CHEMICAL CHARACTERIZATIONS OF CARICA PAPAYA L. FATTY ACIDS AND ESSENTIAL OIL

[1] Turker, E., [2] Gubbuk, H., [3] Ozturk, G., [3] Demirci, B.

[1] Anadolu University, Graduate School of Health Sciences, Department of Pharmacognosy, Eskisehir, Turkey

[2] Akdeniz University, Faculty of Agriculture, Department of Horticulture, Antalya, Turkey

[3] Anadolu University, Faculty of Pharmacy Department of Pharmacognosy, Eskisehir, Turkey

INTRODUCTION:

The genus Carica L. (Caricaceae) is presented by four species in Africa and India, of which Carica papaya L. is the most widely cultivated and best-known species (1). Papaya is known for its food and nutritional values all over the world. and for its food and nutritional values all over the world. Besides, medicinal uses is also common. It is used as antimicrobial, antihelmintic, antifungal, hepatoprotective and diuretic. In this study, it was aimed that analyzed chemical characterization of C. papaya fatty acids and essential oil.

MATERIALS AND METHODS:

Cultivated C. papaya leaves and seeds were supplied from Antalya. The dried and fresh seeds of C. papaya were extracted by Soxhlet appartures to obtaine fatty oils. C. papaya leaves were hydrodistillated for 3 h by Clevenger-type apparatus. The components of essential oil and fatty acids of C. papaya were analysed by GC and GC/MS, simultaneously.

RESULTS:

Oleic acid (72.0, 70.0 %), palmitic acid (15.0, 16.4 %) and linoleic acid (5.3, 5.1 %) were found as the major components of dried and fresh seeds, respectively. Benzyl isothiocyanate (86.3 %), benzene acetonitrile (5.4 %) and phytol (6.3 %) were characterized for the essential oil of C. papaya leaves.

CONCLUSIONS:

Benzyl isothiocyanate was reported for the first time in essential oil of C. papaya (2).

REFERENCES:

1. Krishna KL, Paridhavi M, Patel JA (2008). Natural Product Radiance, 7(4);364-373.
2. Barroso PTW, Carvalho PP, Rocah TB, Pessoa LP, Azevedo DA, Mendes MF (2016). Biotechnology Reports, 11:110-116.

P-064: ANTI-ALZHEIMER ACTIVITY OF SALVIA ARAMIENSIS ROOT EXTRACTS

[1] Alim, G.O., [2] Ozden Yilmaz, T., [1] Yazici Tütünis, S., [1] Tan, N., [1] Miski, M.

[1]Istanbul University, Faculty of Pharmacy, Department of Pharmacognosy, İstanbul, Turkey

[2]Istanbul University, Faculty of Pharmacy, Department of Biochemistry, İstanbul, Turkey

INTRODUCTION:

The Salvia genus is the largest member of the Lamiaceae family. There are about 900 species in the world, 98 of them are grown in Turkey. 58 species are endemic (1). Salvia genus contains diterpenoids, triterpenoids, flavonoids, tannins and phenolic acids (2). Alzheimer's disease is characterised with memory weakness, cognitive dysfunction, behavioral disorders and daily life activity deficits. In addition to this, it is a chronic and progressive neurological disease. Until today, there are no treatments that can stop or prevent the disease. Furthermore, according to the World Health Organization in 2017, approximately 10 million new cases are reported every year. Thus, the discovery and development of new drugs for the treatment of the Alzheimer's disease is extremely important for the social balance of aging society (3). In this study, Salvia aramiensis roots have been investigated. Based on the literature survey, volatile oil and aerial parts extracts of this plant was studied previously for antibacterial, anti-

Alzheimer and antioxidant activities (4). However only limited number of studies were reported on the roots of Salvia aramiensis in Turkey.

MATERIALS AND METHODS:

Anti-Alzheimer activities of various extracts (infusion, decoction, dichloromethane, methanol) from the roots of Salvia aramiensis were studied for the acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) inhibitor activities according the Ellman's method (5).

RESULTS:

Among the extracts of S. aramiensis the highest inhibitory activity against both AChE and BChE was obtained with dichloromethane extract (68.51% and 81.93% at 0.8 mg/mL concentration, respectively) followed by the methanol extract (51.44% and 58.54% at 0.8 mg/mL concentration, respectively). Whereas, infusion and decoction did not show any detectable inhibitor activity on AChE and BChE.

CONCLUSIONS:

Current study confirms the traditional use of Salvia species for the treatment of Alzheimer symptoms. Previous studies suggest that the AChE and BChE inhibitor activity of Salvia species were due to their terpenoid compounds. Thus, a bioactivity directed isolation study is currently in progress to identify the AChE and BChE inhibitor compounds of S. aramiensis root extracts.

REFERENCES:

1. Celep F, Kahraman A, Atalay Z, Doğan M (2014). Plant Systematics and Evolution, 300: 1945-1958.
2. Demirci B, Başer KHC, Yıldız B, Bahçecioğlu Z (2003). Flavour and Fragrance Journal, 18: 116-121
3. World Health Organization. "Dementia, Fact sheet". WHO 2017
4. http://www.who.int/mediacentre/factsheets/fs362/en/
5. Şenol FS, Orhan I, Celep F, Kahraman A, Doğan M, Yılmaz G, Şener B (2010). Food Chemistry, 120: 34-43.
6. Ellman GL, Courtney KD, Andres V, Featherstone RM (1961). Biochemical Pharmacology, 7: 88-95.

P-065: SECONDARY METABOLITE ISOLATION FROM AGRICULTURAL CROP RESIDUES OF HAZELNUT (CORYLUS AVELLANA)

[1] Renda, G., [2] Mutlu, M., [1] Korkmaz, B., [1] Yaylı, N.

[1] Karadeniz Technical University, Faculty of Pharmacy, Department of Pharmacognosy, Trabzon, Turkey

[2] Karadeniz Technical University, Faculty of Pharmacy, Trabzon, Turkey

INTRODUCTION:

Hazelnut (Corylus avellana) which is one of the traditional products of our country, has been exported since the 18th century. More than 300 thousand tons of green crust is obtained per year from C. avellana, thus it has an important place in Turkey's economy (1, 2). At present, hazelnut pests are left on the fields after harvest or used as animal litter. However, there is no study on the purification and recovery of the main ingredients in its composition.

MATERIALS AND METHODS:

Bracts of hazelnuts were dried and powdered and then extracted with methanol. The crude methanol extract was suspended in water and extracted respectively with n-hexane, dichloromethane, ethyl acetate and water to obtain sub-fractions of different polarity. The sub-extracts were studied with various chromatographic methods (column chromatography, vacuum liquid chromatography and medium pressure liquid chromatography). The fractions were collected and monitored with TLC. Those shows the same chromatographic pattern were pooled. 6 compounds were isolated. The structures of the isolated compounds were elucidated by 1 H, 13C-NMR and 2D-NMR spectrometric techniques (1D and 2D).

RESULTS:

The structures of the isolated compounds were determined as; β-amirine: α-amirine: lupeol as a mixture (1,2,3), gamma-taraxasterol (4), kaempferol-3-O-α-L-(4''-E-p-coumaroyl)-rhamnopyranoside (5), kaempferol-3-O-α-L-rhamnopyranoside (6).

CONCLUSIONS:

When the isolated compounds were searched in the literature, it was observed that the kaempferol-3-O-α-L-rhamnopyranoside was previously isolated from C. heterophylla and C. avellana species and the rest of the compounds was previously isolated from C. avellana (3). Future studies are planned to investigate the quantities of these components.

Acknowledgment: This study has been supported by TUBITAK (2209A- Project number: 1919B011701013).

REFERENCES:

1. Oguzkan SB et al., (2016). KSÜ Doga Bilimleri Dergisi, 19: 373-378.
2. Sarımeseli M, Aydogus O (2000). Ankara: Agricultural Economics and Research Institute, 45.
3. Jasicka-Misiak I et al., (2014). Zeitschrift für Naturforschung C, 65: 201-6.

P-066: ESSENTIAL OIL COMPOSITION OF XERANTHEMUM ANNUUM L. FROM TURKEY

[1] Yildiz G., [2] Kose YB., [1] Kurkcuoglu M.

[1] Anadolu University, Faculty of Pharmacy, Department of Pharmacognosy, Eskişehir, Turkey

[2] Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Eskişehir, Turkey

INTRODUCTION:

The genus Xeranthemum L. (Asteraceae) is represented by four species in Flora of Turkey (1). Xeranthemum annuum L. known as 'common immortelle or everlasting flower', is an annual herb widely distributed in Turkey (2). X. annuum is used against burn pains and toothache by mixing with tobacco in the folk medicine of Turkey (3,4). Aim of this study is to determine the essential oil composition of aerial parts of X. annuum collected from Tokat province of Turkey.

MATERIALS AND METHODS:

The aerial parts of X. annuum was distilled with water for 3 h using a Clevenger-type apparatus. The essential oil was analyzed by GC and GC-MS simultaneously.

RESULTS:

The main constituents were identified as hexadecanoic acid (17.7 %), β-pinene (12.6 %), germacrene D (11.7 %), β -caryophyllene (5.9 %) and limonene (4.9 %) in the essential oil.

CONCLUSIONS:

In a study conducted in Greece, β-pinene, (15.2%) β-caryophyllene (8.6%) and γ-muurolene (6.8%) were the main components in the essential oil (5). The present work is the first contribution into the oil composition of X. annuum from Turkey.

REFERENCES:

1. Kupicha FK (1975). In: Davis PH (ed). Flora of Turkey and the East Aegean Islands. Edinburgh University Press, United Kingdom, Vol.5, 604-606.
2. Dogan et al., (2008). Natura Croatica: Periodicum Musei Historiae Naturalis Croatici, 17:193-206.
3. Dirmenci et al., (2006). In Proceedings of the IVth International Congress of Ethnobotany (ICEB 2005) Vol. 167, p. 171.
4. Tuzlaci E (2010). In: Turkish folk medicinal plants, IX: Ovac.
5. Skaltsa et al., (2000). Journal of Essential Oil Research, 12:742-744.

P-067: QUANTITATIVE ANALYSIS OF FLAVONOIDS OF CRATAEGUS MONOGYNA AND CRATAEGUS OXYACANTHA BY HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC)

Ileri , H.K., Ergene Oz, B., Ozbilgin, S., Bahadir Acikara, O., Yaylaci, B., Saltan Iscan,G.

Ankara University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

Crataegus sp. (Hawthorn), which belongs to the family Rosaceae, is comprising approximately 300 species and have been used for the treatment of various diseases such as digestive problems, hyperlipidemia, cardiovascular system disorders in different cultures for many centuries (1,2). Crataegus oxyacantha L. (syn. C. laevigata) and Crataegus monogyna Jacq. are commonly used species in commercial products (3). Major chemical constituents of the leaves, fruits and flowers include flavonoids such as vitexin, hyperoside, vitexin-2- rhamnoside, isovitexin, quercetin (3,4). The main objective of this study was to determine the total flavonoid contents of Crataegus extracts and four commercial products which were prepared using different methods.

MATERIALS AND METHODS:

The dried flowers, leaves and fruits of C. oxyacantha and C. monogyna were extracted with the mixtures of ethanol: water (70:30, 50:50, 45:55) and quantitative analysis (percentage of hyperoside, vitexin-2-O-rhamnoside and total flavonoids expressed as hyperoside) was performed by HPLC. Besides, the hyperoside and vitexin-2-O-rhamnoside contents of four different products supplied from the market were determined using external standard method.

RESULTS:

Our results indicated that total flavonoid contents expressed as hyperoside of the C. oxyacantha and C. monogyna were in the range of 0.5272 to 0.9189%. Vitexin-2-O-rhamnoside and hyperoside amounts in the preparations (C.oxyacantha, C.monogyna and four commercial products) were calculated in the range of 0.1714 to 5.9716%, and 0.0463 to 1.6463%, respectively.

CONCLUSIONS:

In this study hyperoside and vitexin-2-O-rhamnoside contents of Crataegus species and 4 commercial products were determined. According to the results, extraction with 45% ethanol yielded higher flavonoid content and among commercial products, the one in phytosome form was found to involve the highest content by far. These results showed that the highest content of the flavonoid by 45% ethanol extraction was noted in the commercial product which is in the phytosome form.

REFERENCES:

1. Tassel et al., (2010). Pharmacognosy reviews, 4(7):32.
2. Wang et al., (2013). In: Evidence-Based Complementary and Alternative Medicine, 2013.
3. Liu et al., (2011). Food Chemistry, 127(3):1370-1377.
4. Kumar D, Arya V, Bhat Z A, Khan N A, Prasad D N (2012). Revista Brasileira de Farmacognosia, 22(5):1187-1200.

P-068: INHIBITORY EFFECT OF ELAEAGNUS RHAMNOIDES (L.) A. NELSON SUBSP. CAUCASICA ROUSI ON ALPHA-GLUCOSIDASE

[1] Yuca, H., [2] Akcil, B., [1] Ozbek, H., [3] Demirezer, LO., [1] Guvenalp, Z.

[1] Ataturk University, Faculty of Pharmacy, Department of Pharmacognosy, Erzurum, Turkey

[2] Erzincan University, Faculty of Pharmacy, Department of Pharmacognosy, Erzincan, Turkey

[3]Hacettepe University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

The aim of this study is the investigation of antihyperglycemic effect of Elaeagnus rhamnoides (L.) A. Nelson subsp. caucasica Rousi and determination of its phytopharmaceutical potential for treating of Diabetes Mellitus. Elaeagnus belongs to Elaeagnaceae family and it is represented with two species in Turkey. E. rhamnoides is known as “yalancı iğde, çıçırgan” in Turkey. The fruits of the plant are used as constipating, tonic and antiseptic agent. Also fruits are used against influenza and colds due to high vitamin C content in Turkish folk medicine (1). E. rhamnoides has been found to have anticancer, antimutagenic, antioxidant and antibacterial effects in previous studies and to be effective in the treatment of cardiovascular disorders, gastric ulcer, liver damage, burn and atopic dermatitis (2). According to the previous studies, its extracts were found to have flavonoids, proanthocyanidins, vitamins C and E, tocopherols, carotenoids (3). E. rhamnoides subsp. caucasica grows in Anatolia (1). Its fruits are consumed traditionally because of their aphrodisiac and antitussive effects in Elazığ/Turkey (4).

MATERIALS AND METHODS:

In this study, 70% methanol extract and its different polarity fractions (n-hexane, dichloromethane, ethyl acetate, n-butanol and water) prepared from leaves of the plant were evaluated for in vitro α-glucosidase inhibitory activity (5).

RESULTS:

The methanol extract and fractions (ethyl acetate, n-butanol and water) showed inhibitory activities with 10.8% (IC50=0.2632 mg/mL), 93.1% (IC50=0.0456 mg/mL), 92.6% (IC50=0.0494 mg/mL) and 79.0% (IC50=0.0698 mg/mL) values, respectively at 100 µg/mL concentration. n-Hexane and dichloromethane fractions didn’t show any inhibition.

CONCLUSIONS:

The ethyl acetate and n-butanol fractions showed the best α-glucosidase inhibitory activities when compared with the standard compound acarbose that displayed 0.2% inhibitory activity (IC50=2.8488 mg/mL) at 100 µg/mL concentration.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Foundation of Ataturk University (TSA-2018-6447).

REFERENCES:

1. Baytop T (1999). In: Turkiye’de Bitkiler ile Tedavi. Nobel Tıp Kitabevleri, İstanbul, pp 233.
2. Zeb A (2004). Journal of Biological Sciences, 4:687-693.
3. Olas B (2016). Food and Chemical Toxicology, 97:199-204.
4. Cakilcioglu et al., (2011). Ethnopharmacology, 137: 469-486.
5. Tao et al., (2013). Biomedical Chromatography, 27:148-155.

P-069: SCREENING FOR ALPHA-GLUCOSIDASE INHIBITION ACTIVITY OF

PALIURUS SPINA-CHRISTI MILLER

1Yuca, H., 2Akcıl, B., 1Ozbek, H., [3]Demirezer, LO., 1Guvenalp, Z.

[1] Ataturk University, Faculty of Pharmacy, Department of Pharmacognosy, Erzurum, Turkey

[2] Erzincan University, Faculty of Pharmacy, Department of Pharmacognosy, Erzincan, Turkey

[3]Hacettepe University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

The aim of this study is the investigation of antihyperglycemic effect of Paliurus spina-christi

Mill., used in folk medicine for the treatment of hyperglycemia which causes a lot of illnesses, and determination of whether it has phytopharmaceutical potential. Paliurus Mill. belongs to Rhamnaceae family and it is represented with one species in Turkey. P. spina-christi is known as “karaçalı, çaltı dikeni” in our country (1). This species is a very spiky hedge with a height of 2-4 m. The fruits of the plant are used in Turkish folk medicine as antidiabetic, diuretic, constipating agent and against kidney stones. Moreover, it is known that it has been used in the past against eye diseases (2-3). Flavonoids, tannins, amino acids, alkaloids and sterol content (3) in addition to antibacterial and antioxidant activities of this species have been reported (4) in previous studies.

MATERIALS AND METHODS:

In this study, the 70% methanol extract and its different polarity fractions (n-hexane, chloroform, ethyl acetate, n-butanol and water) prepared from fruits of P. spina-christi were evaluated for in vitro α-glucosidase inhibitory activities (5).

RESULTS:

The methanol extract and fractions (n-hexane, chloroform, ethyl acetate, n-butanol and water) showed inhibitory activities with 59.1% (IC50=0.5292 mg/mL), 74.5% (IC50=0.4502 mg/mL), 50.7% (IC50=0.7971 mg/mL), 16.1% (IC50=3.9219 mg/mL), 29.0% (IC50=1.0561 mg/mL) and 73.3% (IC50=0.4765 mg/mL), respectively at 750 µg/mL concentration.

CONCLUSIONS:

The n-hexane and water fractions showed the best α-glucosidase inhibitory activities when compared with the standard compound acarbose that displayed 4.6% inhibitory activity (IC50=2.9438 mg/mL) at 750 µg/mL concentration.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG- 217S206)

REFERENCES:

1. Davis PH (1982). In: Flora of Turkey and the East Aegean Island. Edinburg University Press, UK, pp 523-524.
2. Arituluk ZC, Ezer N (2012). Hacettepe Üniversitesi Eczacılık Fakültesi Dergisi. 32:179-208.
3. Baytop T (1999). In: Türkiye’de Bitkiler ile Tedavi. Nobel Tıp Kitabevleri, İstanbul, pp 244.
4. Kırca A, Arslan E (2008). International Journal of Food Science and Technology. 43:2038-2046.
5. Tao et al., (2013). Biomedical Chromatography, 27:148-155.

P-070: A SURVEY OF OPUNTIA FICUS – INDICA (L.) MILL. FRUITS

[1] Keles, HB., [2] Dogan, Z., [2] Saracoglu, I., [2] Basaran, A.A.

[1]Turkısh Medicines and Medical Devices Agency, Ankara, Turkey

[2]Hacettepe University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

The water extract of Opuntia-ficus indica (L.) Mill. (Cactaceae) is used in folk medicine in South Anatolia (1). The aim of this study is to search antimicrobial activity of Opuntia-ficus indica and isolate new and active compounds.

MATERIALS AND METHODS:

The fruits of Opuntia-ficus indica were collected from Alanya district and water-methanolic extract of the dried and fleshy residue was prefractionated with n-hexane, ethylacetate and n-buthanol respectively. n-butanol, ethylacetate fractions and the water-methanolic extract were tested for antimicrobial activity against to bacteria (E.coli ATCC 25922, E. faecalis ATCC 29212, S. aureus ATCC 29213) and mycetes (C. albicans ATCC 90028, C. krusei ATCC 6258, C. parapsilosis ATCC 90018) with agar microdilution method. Also, we have a serial chromatographic studies on the buthanolic and ethylacetate fractions.

RESULTS:

Four flavonoid glycosides and two flavonoid aglycones were isolated after a serial chromatographic studies on the buthanolic and ethyl acetate fractions. The n-butanol, ethyl acetate fractions and the water-methanolic extract were tested for antimicrobial activity against to bacteria and mycetes. And according to minimum inhibition concentration of fractions they were found active for mycetes.

CONCLUSIONS:

Four flavonoid glycosides and two flavonoid aglycones were isolated after a serial chromatographic studies on the buthanolic and ethyl acetate fractions. Their structural elucidation of the pure compounds were done by 1D- and 2D-NMR analysis and Narcissin (isorhamnetin-3-O-rutinoside), 7-methoxy isorhamnetin-3-O-rutinoside (rhamnazin-3-O-rutinoside), isorhamnetin-3-O-β-galactopyranoside, isorhamnetin-3-O-β-(2’’-O-β-xylopyranosyl-6’’-O-α-rhamnopyranosyl)- glucopyranoside were identified from the buthanolic fraction, while isorhamnetin and 3-O-methyl quercetin were from the ethylacetate fraction. Isorhamnetin-3-O-β-(2’’-O-β-xylopyranosyl-6’’-O-α-rhamnopyranosyl)- glucopyranoside was isolated for the first time from the nature in this study. The NMR data of the isolated known compounds are in good accordance with the references (2, 3).

ACKNOWLEDGEMENTS:

The authors thank to Prof. Dr. Akito Nagatsu, Prof. Dr. Zuhal Guvenalp and Assoc. Prof. Hilal Ozbek for their kind help for recording NMR spectra.

REFERENCES:

1. Keles HB, Yucer R, Catikoglu S, Bacanli M, Basaran N, Basaran AA (2014). Opuntia ficus indica Bitkisi Üzerinde Yapılan Farmakognozik Araştırmalar. Bitkisel İlaç Hammaddesi Bildiri Kitapçığı, 87.
2. Harput US, Genc Y, Saracoglu I (2012). FoodChemToxicol, 50: 1554–1559.
3. Harput US, Saracoglu I, Ogihara Y (2004). Turk J Chem, 28: 761-766.

P-071: EVALUATION OF A-AMYLASE, A-GLUCOSIDASE AND PANCREATIC LIPASE INHIBITION OF TWO PHLOMIS SPECIES

Ekin, H.N., Deliorman Orhan, D., Aslan, M.

Gazi University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

Diabetes mellitus is a chronic metabolic disorder which characterized by hyperglycaemia resulting from defects in insulin mechanism. Obesity is characterized by excess adipose tissue and leads to various chronic diseases. The inhibition of the α-glucosidase and α-amylase enzymes, which play a role in the digestion of carbohydrates, can significantly reduce the postprandial blood sugar increase. Pancreatic lipase inhibition is a focus in obesity treatment due to reduced lipid absorption. The aim of the study is to determine in vitro antidiabetic and antiobesity effects of leaves and flowers of Phlomis grandiflora H. S. Thompson var. grandiflora H. S. Thompson and Phlomis nissolii L.

MATERIALS AND METHODS:

80% Ethanol extracts were prepared. α-Amylase and α-glucosidase enzyme inhibition methods were used to examine antidiabetic activity.Pancreatic lipase inhibition method was used to determine antiobesity activity.

RESULTS:

Our results revealed that P. grandiflora var. grandiflora leaf (84.70±0.78%), flower (95.54±0.41%) extracts and P. nissolii leaf (88.18±0.49%), flower (79.41±0.83%) extracts displayed strong inhibitory activity against α-glucosidase enzyme. All plant extracts displayed lower than 50% α-amylase inhibition. P. nissolii leaf and flower extracts showed pancreatic lipase enzyme inhibitory activity with 25.96±1.74% and 28.34±6.06% values respectively while leaf and flower extracts of P. grandiflora var. grandiflora was ineffective.

CONCLUSIONS:

Our findings indicated that P. grandiflora var. grandiflora and P. nissolii contain potential compounds having selective α-glucosidase inhibitory activity and our work is in progress to identify their active components.

REFERENCES:

1. American Diabetes, A. (2014). Diabetes Care, 37 Suppl 1:81-90.
2. Racette SB, Deusinger SS, Deusinger RH (2003). Physical Therapy, 83:276-288.
3. Liu D, Gao H, Tang W, Nie S (2017). Annals of the New York Academy of Sciences, 1401:28-36.

P-072: SESQUITERPENE LACTONES FROM TANACETUM BALSAMITA L.

[1] Servi, H., [2] Goren, N.,

[1] Altinbas University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Istanbul, Turkey

[2] Yıldız Technical University, Department of Molecular Biology and Genetics, Istanbul, Turkey

INTRODUCTION:

The sesquiterpene lactones have chemo-systematic significance in Asteraceae family. Phytochemical research revealed that sesquiterpene lactones are the principal secondary metabolites in Tanacetum genus. The investigations of Tanacetum L. species are important to find new bioactive compounds, to find out of the species of economic value and the elimination of systematic classification errors of the species (1). Here we report for the first time phytochemistry of ethyl acetate and methanol extracts of Tanacetum balsamita L.

MATERIALS AND METHODS:

Tanacetum balsamita L. collected from Güzeldere-Çuh breach (Van) in Turkey. Comparative phytochemical investigation was carried out on the ethyl acetate and methanol extracts of the plant. The sesquiterpene lactones were isolated and purified by means of chromatographic methods. Structures of isolated compounds were determined by means of spectroscopic methods and some chemical reactions were carried out.

RESULTS:

The extracts of the aerial parts of Tanacetum balsamita yielded a new eudesmanolide; 1α-Acetoxy-3-epi-erivanin, seventeen known sesquiterpene lactones; 1α-Acetoxy-11β(H),13-dihydrodouglanin, Taurin, Artesin, Germacranolide with an 1,5-ether linkage, Artemin, Chrysanthemolide, Santonin, Pallensis, 1,10-epoxyspiciformin, 1-Acetylerivanin, 8α-Hydroxysantamarin, Tamirin, Tavulin, 1α,8α-Dihydroxy-10-epi-arbusculin A, 1α-Hydroxy-desacetylirinol-4α,5β-epoxide, Tanachin and Desacetyl-β- cyclopyrethrosin.

CONCLUSIONS:

Here we report a new sesquiterpene lactone 1α-Acetoxy-3-epi-erivanin isolated from a natural source for the first time. Additionally, sesquiterpene lactones 1α-Acetoxy-11β(H),13-dihydrodouglanin, Chrysanthemolide, pallensis, 1-Acetylerivanin, 1α,8α-Dihydroxy-10-epi-arbusculin A are reported for the first time from Tanacetum genus. These compounds previously isolated from different natural sources.

REFERENCES:

1. Spitzer C, and Steelink C (1966). Sesquiterpene Lactones in Chemotaxonomy, 5:357-365.

P-073: CHEMISTRY OF TANACETUM MUCRONIFERUM HUB.-MOR. & GRIERSON

[1] Servi, H., [2] Goren, N.,

[1] Altinbas University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Istanbul, Turkey

[2] Yıldız Technical University, Department of Molecular Biology and Genetics, Istanbul, Turkey

INTRODUCTION:

Many new compounds with bioactive properties have been identified from Tanacetum L. species. Biological activities of the genus seem to be associated with sesquiterpene lactones, flavonoids, sesquiterpenes, monoterpenes, triterpenes and coumarins (1,2). Due to the various beneficial biological activities, Tanacetum genus attracted the attention of scientists. Here we report phytochemistry of ethyl acetate and methanol extracts of Tanacetum mucroniferum Hub.-Mor. & Grierson for the first time.

MATERIALS AND METHODS:

Tanacetum mucroniferum Hub.-Mor. & Grierson collected from Sakaltutan-Erzincan in Turkey. Comparative phytochemical investigation was carried out on the ethyl acetate and methanol extracts of the plant. The secondary metabolites were isolated and purified by means of chromatographic methods. Structures of isolated compounds were determined by means of spectral methods and some chemical reactions were carried out.

RESULTS:

The extracts of the aerial parts of Tanacetum mucroniferum yielded three new compounds; Mucronolide, Ajanolide A epoxide and 1α,3β,10α-Trihydroxy-7α,11αH-germacra-4-en-12-6α-olide, some known compounds: two sesquiterpene lactones; Arsanin, 9α-Acetoxyartecanin, six flavonoids; Salvigenin, 5-Hydroxy-3′,4′,6,7-tetramethoxyflavone, Cirsilineol, Cirsimaritin, Jaceosidin, 5,3′,4′-Trihydroxy-3,6,7,5′-tetramethoxyflavone, three coumarins; Scoparone, Scopoletin, Umbelliferone and one triterpene; α-Amyrin.

CONCLUSIONS:

Here we report three new sesquiterpene lactones Mucronolide, Ajanolide A epoxide and 1α,3β,10α-Trihydroxy-7α,11αH-germacra-4-en-12-6α-olide isolated from a natural source for the first time. Additionally, we report the flavone 5,3′,4′-Trihydroxy-3,6,7,5′-tetramethoxyflavone for the first time from Asteraceae family and the sesquiterpene lactone 9α-Acetoxyartecanin for the first time Tanacetum genus. These compounds previously isolated from different natural sources.

REFERENCES:

1. 1.Dulger B, Ceylan M, Alıtsaos M, Uğurlu E (1999). Artemisia absinthium L. (Pelin)'un Antimikrobiyal Aktivitesi, 23(3):377-384.
2. Bourgaud F, Gravot A, Milesi S, Gontier E (2001). Production of Plant Secondary Metabolites; A Historical Perspective, 161:839-851.

P-074: ESSENTIAL OIL QUANTITY AND COMPOSITION FROM 4 CULTIVARS OF ORGANICALLY GROWN LAVENDER AND LAVANDIN

[1] Uras, IS., [1] Torun, Z., [1] Pilevneli, AD., [1] Konuklugil, B.

[1] Ankara University, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

Lavender (Lavandula sp.) is a very worthful essential oil plant from the Lamiaceae family. There are 39 lavender species (Lavandula sp.) among them, three[(Lavander (Lavandula angustifolia = L. officinalis = L. vera), Lavandin (Lavandula x intermedia = L. hybrida) Spike lavander (Lavandula spica)] have high commercial value.

Lavander sp. plays an important role in the pharmacology and perfumery industries since it contains essential and aromatic oils. The lavender provides several important essential oils to the fragrance industry including perfumes, colognes, soaps and other cosmetics, flavoring, pharmaceutical, and food industries. Lavandula oil is especially useful for use in nervous system stimulants, sedatives, antibacterial, antifungal, carminative (smooth muscle relaxing), and effective for burns and insect bites [1-4].

In this study, we compared essential oil quantity and quality of 4 cultivars of certified organically grown lavender (Lavandula sp).

MATERIALS AND METHODS:

The composition of the essential oils obtained from dried aerial parts of four Lavandula sp., were analyzed by GC, GC-MS. Fifteen compounds have been identified in these essential oils.

1. *Lavandula angustifolia* var. Drujba
2. *Lavandula angustifolia* var. Sevtopolis
3. *Lavandula angustifolia* var. Yubileina
4. *Lavandin L.x intermedia* var. Super A

RESULTS:

Lavandin cultivars (Lavandula x intermedia Super A.) produced significantly higher oil yield (5 %)) compared to three lavender cultivars (2-2,5 %). The major constituents of the oil of Lavender 1, 2 and 3 were linalool (18-14,82-16,71 %) and 1,8 cineol in Lavender 4 (16,82 %).

CONCLUSIONS:

Our results demonstrate that organically-grown lavender and lavandin in Southeastern Anatolia region. The essential oils obtained from these lavender species are commercially evaluated.

REFERENCES:

1. Hui et al., (2010). African Journal of Microbiology Research. 4(4) : 309-313.
2. Venskutonis et al., (1997). Journal of Essential Oil Research. 9(1):107-110.
3. Cavanagh, H., J.M. Wilkinson, (2002). Phytotheraphy Res. 16, 301-308.
4. Adam et al., (1998). J. Agric. Food Chem. 46:1739–1745

P-075: VOLATILE COMPOSITION OF SERAPIAS ORIENTALIS SUBS. ORIENTALIS

[1] Erik, I., [1] Korkmaz, B, [2] Terzioglu, S., [1] Yayli, N.

[1]Karadeniz Technical University, Faculty of Pharmacy, Department of Pharmacognosy, Trabzon, Turkey

[2]Karadeniz Technical University, Faculty of Forestry, Department of Forest Botany, Trabzon, Turkey

INTRODUCTION:

Serapias L. is a genus of Orchidaceae family, which occurs naturally from the east-central and eastern Mediterranean to the western Transcaucasus that was represented by 30 cosmopolite taxa (1). Some of the Orchidaceae species have been used as herbal medicine. In the literature, volatile constituent analyses of Serapias L. species were not mentioned. In this work, volatile components and solvent extracts (n-hexane, methanol and water) obtained from Serapias orientalis subsp. orientalis were investigated by SPME GC-FID/MS (2-4).

MATERIALS AND METHODS:

The plant (S. orientalis subsp. orientalis) used in the study was collected from the Karadeniz Technical University Campus (115 g, fresh) at an altitude of 130 meters. Identification of the plant was made by Prof. Dr. Salih Terzioğlu and herbarium number was given. Solvent extracts, SPME Method were performed according to the literature.

RESULTS:

SPME GC-FID/MS analyzes for the fresh plant and solvent extract (n-hexane, methanol, and water) of S. orientalis subsp. orientalis revealed 7, 12, 7, and 4 natural compounds with in the ratio of 99.7% to 100.0%, respectively. Limonene (76.6%, 41.8%, 61.6%, and 45.4%) was found to be major compound in the SPME of the fresh plant and SPME of the n-hexane, methanol and water extracts of S. orientalis subsp. orientalis, respectively. SPME of the methanol extract of it revealed p-methoxymethylphenol (52.9%) as main component.

CONCLUSIONS:

Limonen was the major compound of all there extraction method (SPME, n-hexane, and methanol) obtained from fresh S. orientalis subsp. orientalis in the range of 41.8% to 76.6%. However, p-methoxymethylphenol was found as a major component only in methanol extract of the plant. This clearly showed that various extraction methods that was used in this work gave the identification of different components as in the literature.

REFERENCES:

1. Pellegrino G, Bellusci F, Palermo AM (2017). , Ecology and Evolution, 7: 7171–7177.
2. Adams RP, Morris JA, Pandey RN, Schwarzbach AE (2005). Biochem. Syst. Ecol., 33 (8): 771-787.
3. Yanez X, Pinzon ML, Solano F, Sanchez LR (2002). McVaugh, Molecules, 7(9): 712-716.
4. Boylston TD, Viniyard BT (1998). Isolation of volatile flavor compounds from peanut butter using purge-and-trap technique in Instrumental Methods in Food and Beverage Analysis, Wetzel D, Charalambous G, ed(s)., pp 225-243.

P-076: ESSENTIAL OIL AND SPME ANALYSIS OF IPOMEA PURPUREA

Erik, I., Korkmaz, B., Yayli, N.

Karadeniz Technical University, Faculty of Pharmacy,Trabzon, Turkey

INTRODUCTION:

The genus Ipomoea comprises the largest number of species (500-600 species) within the Convolvulaceae (1) and found throughout subtropical and tropical regions of the world. Several species of Ipomoea have been used as an herbal medicine to treat rheumatism, hydrocephaly, diabetes, hypertension, dysentery, fatigue, arthritis, meningitis, and kidney ailments etc. Some of these species showed various biological activities such as antimicrobial, anticancer, anti-inflammatory, analgesic, hypotensive, spasmolitic, and anticoagulant. Phenolic, glycolipids, and alkaloid type compounds were the most common active natural components mentioned from these plant extracts. In the literature, essential oil (EO) and SPME analyses of Ipomea purpurea were not mentioned. In this work, essential oil, wet and dry SPME of I. purpurea were investigated by GC-FID/MS (2-4).

MATERIALS AND METHODS:

The plant (I. purpurea) used in the study was collected from the Şinik-Akçaabat, Trabzon (215 g, wet) at a height of 355 meters. Identification of the plant was made by Prof.Dr. Salih Terzioğlu and herbarium number was given. EO analysis and SPME method were done according to the literature.

RESULTS:

GC-FID/MS analyzes for EO,SPME for the fresh and dry plant of I. purpurea have revealed 33, 12, and 11 natural compounds within the ratio of 79.1%, 99.6% and 99.4%, respectively. Caryophyllene oxide (30.6%), germacrene-D (28.2%), and trans-(β)-caryophyllene (22.5%) were the major component in the EO of I. purpurea. D-limonene (42.1% and 42.6%) and germacrene-D (34.2% and 33.6%) were the main compounds in both wet and dry I. purpurea, respectively.

CONCLUSIONS:

Terpenes and terpenoids constituent of I. purpurea were the major class of compounds. Wet and dry SPME analysis of I. purpurea gave almost the same compounds with small differentiation in the ratio.

REFERENCES:

1. Austin DF, Huaman Z (1996). Taxon 45:3-38.
2. Sahayaraj K, Kombiah P, Dikshit AK, Rathi JM (2015). Journal of the Serbian Chemical Society. 80:465-473.
3. Majetic BCJ, Rausher MD, Raguso RA (2010). South African Journal of Botany. 76: 632-642.
4. Schimming T, Jenett-Siems K, Mann P, Tofern-Reblin B, Milson J, Johnson RW, Deroin T, Austin DF, Eich E (2005). Phytochemistry. 66:469-480.

P-078: EVALUATION OF ANTIMICROBIAL ACTIVITY IN SECONDARY METABOLITES FROM PLECTRANTHUS ZEYLANICUS: A SEARCH FOR NOVEL DISINFECTANTS

[1] Napagoda, M., [1] De Soyza, S., [2] Qader, M., [3] Lorenz, S., [3] Schneider, B., [3] Svatoš, A., [1] Wijayaratne, G., [1] Nagahawatte, A., [2] Jayasinghe, L.

1 University of Ruhuna, Faculty of Medicine, Galle, Sri Lanka

2National Institute of Fundamental Studies, Kandy, Sri Lanka

3Max Planck Institute for Chemical Ecology, Jena, Germany

INTRODUCTION:

Plectranthus zeylanicus Benth (Lamiaceae), is a perennial herb widely utilized in Ayurvedic and folk medicine in Sri Lanka for thousands of years (1). Although the plant is traditionally used as an antimicrobial remedy, its pharmacological features and the phytochemistry have not been comprehensively explored yet to rationalize the reported ethnobotanical significance. Therefore, the present study was undertaken to evaluate the antimicrobial potential of different extracts of P. zeylanicus and to characterize the bioactive phytochemicals thereof.

MATERIALS AND METHODS:

Organic extracts prepared from the whole plants of P. zeylanicus were tested against Gram positive and Gram negative bacteria; Enterococcus faecalis, Staphylococcus aureus, Staphylococcus saprophyticus, Escherichia coli, *Pseudomonas aeruginosa*, Salmonella serotype Typhi and nine clinical isolates of methicillin-resistant Staphylococcus aureus (MRSA). Besides, the antifungal activity was evaluated against the opportunistic fungal pathogen, Candida albicans. Disc diffusion and broth micro-dilution methods were employed in the determination of the antimicrobial activity of these extracts. Based on the preliminary observations, the most active extract was subjected to activity guided fractionation and the isolated compounds were extensively studied for the antimicrobial activity. Furthermore, the quantitative surface disinfectant assay was employed to determine the disinfectant potential of the compounds against MRSA strains on smooth and rough surfaces.

RESULTS:

A potent antimicrobial activity was observed in dichloromethane extract, hence subjected to the activity guided fractionation. The extract was also analyzed by gas chromatography coupled mass spectrometry, and it revealed the presence of phytosterols, fatty acids, sesquiterpenes, acyclic diterpenes and several other metabolites. Among the compounds isolated from this extract, the structure of the most active compound was elucidated as 7α-acetoxy-6β-hydroxyroyleanone by liquid chromatography coupled mass spectrometry and nuclear magnetic resonance data. This compound displayed a prominent antibacterial activity especially against S. aureus, S. saprophyticus, *P. aeruginosa* and MRSA isolates with a minimum inhibitory concentration (MIC) in the range of 31.25-250 µg/mL. Furthermore, the compound has inhibited the growth of C. albicans and also exhibited a significant disinfectant potential against MRSA isolates in comparison to the commercially available disinfectants.

CONCLUSIONS:

The MIC values observed as 31.25 µg/mL for 7α-acetoxy-6β-hydroxyroyleanone was significantly better than the MIC values reported in literature for most of the ubiquitous phyto-constituents. Further studies on disinfectant activity and self-assembly properties of the isolated secondary metabolites are in progress in the pursuit of new antimicrobial/ disinfectant agents.

ACKNOWLEDGEMENTS:

The study was supported by NSF-Sri Lanka (Research Grant RG/BS/2015/01)

REFERENCES:

1. Jayaweera, DMA.(1982). In: Medicinal plants (Indigenous and exotic) used in Ceylon, Part III. National Science Council, Sri Lanka, pp.108-109.

P-079: INHIBITORY EFFECT OF ANCHUSA STRIGOSA BANKS & SOL. ON 5-LIPOXYGENASE ENZYME IN VITRO

[1] Icen, M.S., [2] Temel, H.E., [3] Gurbuz, I., [4] Demirci, F.

[1]Inönü University, Faculty of Pharmacy, Department of Pharmacognosy, Malatya, Turkey

[2]Anadolu University, Faculty of Pharmacy, Department of Biochemistry, Eskisehir, Turkey

[3]Gazi University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

4Anadolu University, Faculty of Pharmacy, Department of Pharmacognosy, Eskişehir, Turkey

INTRODUCTION:

Anchusa strigosa, a member of the Boraginaceae family, is distributed in temperate climatic regions, especially in the tropical zone and in the Mediterranean (1). The aerial parts of Anchusa strigosa were used in digestive disorders and cancer treatment as folk medicine in Turkey (2, 3). Phytochemical studies on Anchusa strigosa have shown that pyrrolizidine alkaloids and phenolic compounds were isolated from the roots (4).

MATERIALS AND METHODS:

The roots of the Anchusa strigosa were collected in Malatya, cleaned and then sliced into small pieces and dried. Methanol extract was prepared for activity studies. n-Hexane, dichloromethane, ethyl acetate, n-butanol and residual aqueous fraction were obtained from the methanol extract respectively, by liquid-liquid fractionation. The extract and fractions were applied to the 5-lipoxigenase (5-LOX) inhibition assay. The determination of 5-LOX (soybean) inhibition levels of all samples was performed according to the reference method with a spectrophotometric kinetic method adapted to some modifications (5).

RESULTS:

As a result, when the percentages of inhibition on the enzyme of the liquid-liquid fractions and the methanolic extract were evaluated, it was found that the ethyl acetate fraction inhibited 67.96% of the enzyme at 100 µg / ml with the highest activity. Serial dilutions from the ethyl acetate fraction were prepared for determining the IC50 value, the IC50 value was determined to be 40.875 µg / ml. Nordihydroguaiaretic acid (NDGA) was used as the standard reference and the IC50 value was determined to be 6.95 µg / ml.

CONCLUSIONS:

According to our results, Anchusa strigosa may be a potential source for obtain an anti-inflammatory drug. Our further studies are in progress.

ACKNOWLEDGEMENTS:

This study was financially supported by The Scientific and Technological Research Council of Turkey – TUBİTAK (Project no: SBAG-214S129).

REFERENCES:

1. Al-Snafi, A. (2014). International Journal of Pharmacy and Pharmaceutical Sciences, 6: 7-10.
2. Polat et al., (2013). Journal of ethnopharmacology, 148: 951-963.
3. Akgul et al., (2018). Journal of ethnobiology and ethnomedicine, 14: 12-30.
4. Braca et al., (2003). Planta medica, 69: 835-841.
5. Baylac S, Racine P (2003). International Journal of Aromatherapy, 13: 138-142.

P-080: DETERMINATION OF PHENOLIC CONSTITUENTS FROM MARRUBIUM HETEREDON (BENTH.) BOISS. & BALANSA USING LC-MS/MS

[1] Icen, M.S., [2] Goger, F., [3] Arabaci, T.,[4] Dirmenci, T., [5] Baser, K.H.C.

[1]Inönü University, Department of Pharmacognosy, Malatya, Turkey.

[2]Anadolu University, Department of Pharmacognosy, Eskisehir, Turkey.

[3]Inönü University, Department of Pharmaceutical Botany, Malatya, Turkey.

4Balıkesir University, Department of Biology Education, Balıkesir, Turkey.

5Near East University, Department of Pharmacognosy, Lefkosa (Nicosia), Northern Cyprus, Turkey.

INTRODUCTION:

The genus Marrubium has a common traditional usage such as, pulmonary infections, inflammation and hypotension, as cholagogue and sedative agent, and for pain relief. It contains several diterpenoids (e.g. marrubiin) and phytochemical constituents comprise mainly diterpenes, polyphenols, steroids, phenylpropanoids and flavonoids with important biological properties (1).

MATERIALS AND METHODS:

Aerial parts of Marrubium heterodon (Local name: Kınalı Kekik) were collected at flowering stage from Bolkar mountain, Niğde-Turkey. The aqueous, methanolic and ethyl acetate extracts were obtained by macerating plant materials for 3x24h. Experiments were performed with a Shimadzu 20A HPLC system coupled to an Applied Biosystems 3200 Q-Trap LC-MS/MS instrument equipped with an ESI ion source was used in the negative ionization mode. Separations were performed on an ODS 150 x 4,6 mm, i.d., 3 µm particle sizes, octadecyl silica gel analytical column operating at 40ºC at a flow rate of 0.5ml/min.

RESULTS:

According to the LC-MS/MS analysis, Anisofolin is the only compound determined in the ethyl acetate extract which was previously identified in Marrubium vulgare (2). Main compound of the ethyl acetate extract was determined as a quercetin derivative. Methanol extract was found to be rich in phenyl propanoid and flavonoid derivatives. Kaempferol rutinoside and rutin were determined in the aqueous extract.

CONCLUSIONS:

The compounds we have identified in Marrubium heteredon have also been detected in other Marrubium species. The pharmacological activity of the identified compounds may be indicative of the noteworthy conclusion of the biological activity studies to be performed on this endemic species.

REFERENCES:

1. Meyre Silva C and Cechinel Filho V (2010). Curr Pharm Desig, 16: 3503-3518.
2. Amessis Ouchemoukh et al. (2014). Ind Crop Prod, 61: 120-129.

P-081: ANTIOXIDANT CAPACITY, TOTAL PHENOLIC AND FLAVONOID CONTENTS OF POLYGONUM EQUISETIFORME SIBTH. & SM.

[1] Uzun, M., [1] Yuzbasioglu Baran, M., [2] Arituluk, Z.C., [1] Kuruuzum Uz, A.

[1]Hacettepe University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

[2]Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

INTRODUCTION:

The genus Polygonum (Polygonaceae) contains about 300 species in the world. It consists of 41 species as 7 of them endemic in Turkey (1). Some species possess antioxidant, antitumor and antidiabetic effects, etc. Numerous Polygonum species are frequently used as food, as well as in traditional medicine. Some of the secondary metabolites identified in the species of the Polygonum genus are flavonoids, anthraquinones, stilbenes, terpenes, tannins and lignans (2).This study was focused on the determination of the total phenolic and flavonoid contents together with antioxidant capacity of Polygonum equisetiforme Sibth. & Sm.

MATERIALS AND METHODS:

Methanol extract of the aerial parts of P. equisetiforme was dissolved in water and partitioned with petroleum ether. Aqueous extract was subjected to polyamide coloumn to give six main fractions.Total phenolic and flavonoid content of extracts and fractions were measured by Folin-Ciocalteau and AlCl3 assays (3). Determination of in vitro antioxidant capacity of samples are done by DPPH, ABTS,NO, SO, FRAP and CUPRAC assays.

RESULTS:

Total phenolic content was measured as 835.9 mg gallic acid/100 g material for fraction 16-18 and total flavonoid content was measured as 284.6 mg quercetin/g for fraction 16-18. IC50 values for DPPH, NO and SO assays measured as 18.88 µg/ml for fraction 5-8, 104.37µg/ml for fraction 23-28 and 12.87µg/ml for fraction 9-12 respectively. CUPRAC, FRAP and ABTS antioxidant capacities were measured as 797.9 mg gallic acid/g for fraction 23-28, 826.9 mg trolox/g for fraction 16-18, 448.6 mg trolox/g for fraction 16-18 respectively.

CONCLUSIONS:

Fraction 16-18 shows the highest antioxidant capacity, total phenolic and flavonoid contents. Fractions 9-12 and 23-28 have promising antioxidant capacities. Further studies will continue on these highly effective fractions.

ACKNOWLEDGEMENTS:

This work was supported by the Hacettepe University Scientific Research Projects Coordination Unit(THD-2017-11469).

REFERENCES:

1. Coode MJE, Cullen J (2000). In:Guner., et al. (ed). The Flora of Turkey and East Aegean Islands. Edinburgh University Press, Edinburgh, pp 54-56.
2. Dawidar AM, et al., (2014). Research Journal of Pharmaceutical, 5:140-148.
3. Zhang Q, Zhang J et al., (2006). Journal of Applied Phycology, 18:445–450.
4. Büyüktuncel E (2013). Marmara Pharmaceutical Journal,17:93-103.
5. Apak R, Güçlü K et al., (2006). International Journal of Food Sciences and Nutrition, 57: 292-304.

P-082: COMPARISON OF DIFFERENT EXTRACTION TECHNIQUES WITH REGARD TO THE ANTI-INFLAMMATORY ACTIVITY OF ASPARAGUS OFFICINALIS

[1] Karacaoglu, M., [2] Yilmaz Sarialtın, S., [1] İscan Saltan, G. H., [2] Coban, T.

[1] Ankara University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

[2] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Ankara, Turkey

INTRODUCTION:

Asparagus (*Asparagus officinalis* L., Liliaceae) spears which widely consumed all over the world, are highly valued for their abundance of bioactive compounds such as saponins, flavonoids, hydroxycinnamic acids, sterols, fructan, carotenoids, and amino acids (1). According to the literature, *A. officinalis* is an herbal medicine with remarkable antioxidant, anti-inflammatory, and antihepatotoxic, antitumor, and anti-diabetic activities as well as possessing hypocholesterolemic, hypotensive and renal protective properties (1, 2). The objective of this investigation was, to evaluate the influence of different cultivation region on the anti-inflammatory activity and chemical profile of Asparagus officinalis.

MATERIALS AND METHODS:

Fresh Asparagus spears were purchased from a supermarket, in Turkey. Ethanolic extracts of A. officinalis, cultivated in Peru(P) and Turkey(T) obtained with different extraction techniques such as maceration, soxhelet apparatus. The in vitro anti-inflammatory effects of the extracts (P, T1, and T2) were determined by applying HRBC method; reference chemically acetylsalicylic acid.

RESULTS:

All extracts exhibited in vitro anti-inflammatory activities with different IC50 values ranging from 2.63 to 9.16 mg/ml. The results showed that the extract of samples cultivated from Turkey and obtained by using soxhlet technique was the most effective when compared with the other extracts.

CONCLUSIONS:

According to the results of current study, the extract prepared by using soxhlet apparatus exhibited better anti-inflammatory activity. This result suggests that soxhlet extraction yielded higher content of the components which are responsible for the anti-inlammatory activity of the plant.

REFERENCES:

1. Lee EJ, Yoo KS, Patil BS (2010). Journal of Food Science, 75(9).
2. Jiménez-Sánchez C, Lozano-Sánchez J, Rodríguez-Pérez C, Segura-Carretero A, Fernández-Gutiérrez A (2016). Journal of Food Composition and Analysis, 46: 78-87.

P-083: THERAPEUTIC AND ECONOMIC ASPECTS OF CYANOBACTERIA FROM GEOTHERMAL SOURCES IN AFYONKARAHISAR PROVINCE

[1] Sensoy, M. , [1] Dogan, Z., [2] Conk Dalay, M., [2] Demirel, Z.,[1] Saracoglu, I.

[1]Hacettepe University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

[2]Ege University, Faculty of Engineering, Department of Bioengineering, Izmir, Turkey

INTRODUCTION:

Microalgae and Cyanobacteria are prominent microorganisms with their unique features. Cyanobacteria, itself, and their metabolites are potentially of therapeutical importance, such as antiviral, immune-modulators, inhibitors (such as trypsin, plasmin, thrombin, chymotrypsin inhibitor etc.), or cytostatics and the most important cyanobacteria is Spirulina platensis biotechnologically (1, 2). C-phycocyanin is one of the major biliproteins in S. platensis, which has high commercial value as natural dye but an increasing number of investigations have shown on its health promoting properties and broad

range of pharmaceutical applications (3). In this study, four cyanobacteria were isolated from three different geothermal sources from Afyonkarahisar. Our aim is to investigate these species for their therapeutically active bioproducts, which have commercial potential, as an alternative of S. platensis.

MATERIALS AND METHODS:

DNA analyses of cyanobacteria were made in Refgen Gene Research and Biotech. Co. in Turkey. HPLC-DAD system was used for determination of carotenoid profiles. C-phycocyanins were isolated by using stepwise chromatography methods and were compared with standard C-phycocyanin with SDS-Page (4). Antioxidant activity was determined with DPPH and cytotoxic activity experiments were also conducted against HEp-2 cell line by MTT assay (5).

RESULTS:

Strains were determined as Geitlerinema sp. (M1), Oscillatoria sp. (M2) and two Leptolyngbya sp. (M3 and M4). HPLC-DAD showed that lutein is a major carotenoid in all species. C-phycocyanin was isolated with highest yield (36%) from freeze-dried M3 biomass. M3 extracts showed highest cyctotoxic (IC50 =66 µg/ml) and antioxidant activity (IC50 =68,52 µg/ml), among other strains.

CONCLUSIONS:

Globally, alternative therapeutic and nutritive source seeking is increasing. Leptolyngbya sp. (M3) can be an alternative of Spirulina sp. market with its bioactive compounds for humans' health and nutrition.

REFERENCES:

1. Pulz O, Gross W (2004). Appl Microbiol Biotechnol, 65:635-648.
2. Skulberg OM (2000). J Appl Phycol, 12:341-348.
3. Spolaore P, Joannis Cassan C, Duran E, Isambert A (2006). Journal of Bioscience and Bioengineering, 101: 87-96.
4. Herrera A, Boussiba S, Napoleone V, Hohlberg A (1989). J of Appl Phycol, 1: 325-331.
5. Harput S, Genc Y, Saracoglu I (2012). Food Chem Toxicol, 50: 1554-1559.

P-084: DETERMINATION OF ANTIAGING POTENTIAL OF RUMEX CRISPUS' MAIN COMPOUNDS BY MOLECULAR DOCKING STUDIES

Uzun, M., Demirezer, LO.

Hacettepe University, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

MMP-1, MMP-8 and MMP-13 enzymes are interstitial collagenases and play an important role in the breakdown of collagenase, which provides skin youth and tightness (1). Rumex species (Polygonaceae) have various biological effects and contain anthranoids, tannins, flavonoids and naphthalenes as main secondary metabolites (2-4). In this study, we aimed to determine the MMP inhibitory activities of these secondary metabolite skeletons by molecular docking method.

MATERIALS AND METHODS:

AutoDock-Vina 1.5.4 program (5) was used as the basic docking software for docking calculations. RCSB Protein Data Bank, PDB Sum, SDSC Biology Work Bench, Notepad++, Discovery Studio 3.5 Client, MGLTools 1.5.4, VMD 1.9, Pymol programs have been used as utilities. MMP-1, MMP-8 and MMP-13 enzymes were selected as targets, tannin, flavone, naphthalene and anthraquinone skeletons were selected as ligands. The target MMP-1, MMP-8 and MMP-13 enzymes were constructed with pDB:966C, pdb:1BZS and pdb:3ZXH codes, respectively. 3-D structures of ligands were drawn with Discovery Studio 3.5 Client. Docking simulations between ligands and targets were repeated 50 times.

RESULTS:

The binding energies were found as: to MMP-1; tannin (-9.9 kcal/mol), flavonoid (-8.5 kcal/mol), antrhraquinone (-7.5 kcal/mol), naphthalene (-6.7 kcal/mol) , to MMP-8; tannin (-10.3 kcal/mol), flavonoid (-9.5 kcal/mol), naphthalene (-7.4 kcal/mol), antrhraquinone (-6 kcal/mol), to MMP-13; tannin (-8 kcal/mol), flavonoid (-7.9 kcal/mol), antrhraquinone (-7.6 kcal/mol) and naphthalene (-6.3 kcal/mol).

CONCLUSIONS:

According to the results of molecular docking studies, all of the ligands have lower binding energies (< -2 kcal / mol), which shows they could inhibit MMP-1, MMP-8 and MMP-13 enzymes. Molecular docking studies of anthranoid, tannin, flavonoid and naphthalene skeletons on MMP-1, MMP-8 and MMP-13 enzymes were carried out for the first time.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-214S147)

REFERENCES:

1. Chung JH, Hanft VN, Kang S (2003). Journal of the American Academy of Dermatology, 49(4): 690-697.
2. Saleh NAM, Elhadidi N, Arafa RFM (1993). Biochemical Systematics and Ecology, 21(2): 301-303.
3. Demirezer LO, Kuruuzum A, Bergere I, Schiewe HJ, Zeeck A (2001). Phytochemistry, 56(4): 399-402.
4. Demirezer LO, Kuruuzum A, Bergere I, Schiewe HJ, Zeeck A (2001). Phytochemistry, 58(8): 1213-7.
5. Trott O, Olson AJ (2010). Journal of Computational Chemistry, 31(2): 455-461.

P-085: THE ROLE OF RUMEX CRISPUS EXTRACTS ON MATRIX METALLOPROTEINASE-13 (MMP-13) ENZYME INHIBITION AGAINST SKIN AGING

Uzun, M., Demirezer, LO.

Hacettepe University, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

MMPs (Matrix Metalloproteinases) are called proteolytic enzymes and responsible for breaking down extracellular matrix and cause of cell-aging (1). A member of this family MMP-13 play an important role in the breakdown of collagenase, thus causing premature aging of the skin (2-3). Therefore inhibition of MMP-13 enzyme should be a part of treatment strategy in skin aging. In this study, we aimed to determine the MMP-13 inhibitory activities of Rumex crispus L. (Polygonaceae) extracts.

MATERIALS AND METHODS:

Standardized n-hexane, dichloromethane, ethyl acetate, ethanol and ethanol:water (70:30) extracts were prepared from roots, leaves and fruits and inhibitory effects on MMP-13 were investigated. MMP-13 inhibitor screening assay kit -including microplate, MMP-13 enzyme (3.45 U/ µl), MMP inhibitor (1.3 mM NNGH in DMSO), MMP substrate (25 mM in DMSO) and colorimetric assay buffer- was used. NNGH was used as potent MMP-13 inhibitor. Inhibitor activities of all extracts were measured in 50 µg/mL, 100 µg/mL, 200 µg/mL, 300 µg/mL, 400 µg/mL and 800 µg/mL concentrations at 412 nm.

RESULTS:

The aqueous alcoholic extracts showed the highest inhibitory effect among other extracts at all concentrations. Inhibition values were 87.08% for root extracts, 85.41% for leaf extracts and 89.38% for fruit extracts, while NNGH was 91.94%.

CONCLUSIONS:

The MMP-13 inhibitor acitivities of Rumex crispus L. extracts were first determinated. This study shows that aqueous alcoholic extracts of Rumex crispus L. may be potential novel MMP-13 inhibitors and may fight against skin aging.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-115S564).

REFERENCES:

1. Wojtowicz Praga SM, Dickson RB, Hawkins MJ (1997). Investigational New Drugs, 15(1): 61-75.
2. Chung JH, Hanft VN, Kang S (2003). Journal of the American Academy of Dermatology, 49(4): 690-697.
3. Mukherjee PK, Rai S, Kumar V, Mukherjee K, Hylands PJ and Hider RC (2007). Expert Opinion on Drug Discovery, 2(5): 633-657.

P-087: PHYTOCHEMICAL INVESTIGATIONS ON ROOTS OF RUMEX ACETOSELLA L.: ISOLATION OF A NEW COMPOUND

[1] Ozenver N., [2] Kauhl U., [2] Opatz T., [3] Efferth T., [1] Demirezer LO.

[1]Hacettepe University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

[2]Johannes Gutenberg University, Institute of Organic Chemistry, Mainz, Germany

[3]Johannes Gutenberg University, Institute of Pharmacy and Biochemistry, Department of Pharmaceutical Biology, Mainz, Germany

INTRODUCTION:

Rumex acetosella L. is a member of Rumex genus from Polygonaceae family and widely distributed over the world with a wide scale of traditional usage (1).

MATERIALS AND METHODS:

We used various chromatography techniques to view phytochemical profile of Rumex acetosella. In this respect, roots of R. acetosella were extracted with methanol, which was subjected to diverse column chromatographies based on different seperation techniques for isolation of pure compounds. Following isolation of the pure compounds, the structures of which were identified based on the spectroscopic data such as IR, Mass and NMR spectra.

RESULTS:

As a result of phytochemical studies, total of 12 compounds in which one as a new compound were elucidated on the basis of spectroscopic data. Structures of those compounds were identified as (E)-piceid (a stilbene derivative), ethanone, 1-[2-(β-glucopyranosyloxy)-4-hydroxy-6-methylphenyl)] (an ethanone derivative), nepodin-

8-O-β-glucoside (naphthalene derivative), catechin (tannin derivative), lyoniside and isolariciresinol-9-O-β-xyloside (lignan derivatives), a mixture of rumejaposide G and rumejaposide H, emodin, emodin-8-O-β-glucoside, a mixture of chrysophanol-8-O-β-glucoside and physcion-8-O-β-glucoside (anthranoid derivatives). IR spectrum of new compound pointed out the presence of aromatic C=C (1464, 1605 cm-1), aromatic C-H (3000-3100 cm-1), alkane C-H (1328, 2928 cm-1), C-C (944, 1023 cm-1), O-H (3300-3650 cm-1), C-O (1077, 1173 cm-1), and C=O (1654 cm-1) functions. For the new compound, 1H-NMR spectrum indicated H atoms with their integrating proton signals, while 13C-NMR spectrum detected the data of carbon atoms in the structure. Additionally, COSY spectrum presented H signals coupled with each other. HMQC spectrum exhibited H atoms and their binding carbons in the structure, whereas HMBC displayed long-range couplings between protons and carbons in the molecule. Following the analysis of NMR spectra, molecular formula of the new compound was detected as C15H20O8, which was further confirmed by HR-MS (ESI) m/z as [M+Na] + 351.1047.

CONCLUSIONS:

The structures of the compounds isolated from R. acetosella roots were identified based on spectroscopic data in the literature. The structure of the new compound was checked in the literature, as well; however any substance with those data was found. Therefore, the new compound as an ethanone derivative was named as acetoselloside.

REFERENCES:

1. Vasas A, Orban-Gyapai O, Hohmann J (2015). J Ethnopharmacol, 175: 198-228.

P-088: ANTIMICROBIAL ACTIVITIES OF CEPHALARIA PROCERA FISCH. & AVÉ-LALL. IN TURKEY

[1] Mataraci Kara, E., [2] Yazici Bektas, N., [3] Yesil, Y.

[1] İstanbul University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Istanbul, Turkey

[2] Istanbul University, Faculty of Pharmacy, Department of Pharmacognosy, Istanbul, Turkey

[3]Istanbul University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Istanbul, Turkey

INTRODUCTION:

The genus Cephalaria Schrad. ex Roem. (family Caprifoliaceae) comprises about 94 species, which are widespread, mainly in the Mediterranean region and the Middle East. Cephalaria is represented by 39 species in Turkey (3). Cephalaria procera Fisch. & Avé-Lall. is called as Ganteper, Gulinga and Cevrük and its stems are used for wound healing and antihemorhagic in Turkey (4). This study aims to investigate the antimicrobial activites of the several extracts obtained from aerial parts of C. procera species.

MATERIALS AND METHODS:

The whole plants of C. procera were collected from Eastern Turkey (Erzurum) in July 2017 by Dr. Yeter Yeşil, Nurdan Yazıcı Bektaş and Burak Bektaş; identified by Dr. Yeter Yeşil. These specimens were stored at the Herbarium of Istanbul University (ISTE 115 326, ISTE 115 327). The aerial part of C. procera was extracted with methanol at room temperature for overnight three times. The methanol extract was concentrated under reduced pressure. The methanol extract was solved with distilled water and extracted with n-buthanol. N-buthanol extract was dried and extracted with n-hexane. By this way methanol, water, n-buthanol and n-hexane extracts were obtained (5). Antimicrobial activity was analyzed using a microdilution assay against several microorganisms (1, 2).

RESULTS:

According to our results, it is observed that n-hexane extract exhibited antifungal activity with the lowest MIC (156.2 µg/mL) value against tested Candida tropicalis. Also, n-hexane and n-buthanol extracts showed antibacterial activity with the lowest MIC (312.5 µm/mL) value against Escherichia coli.

CONCLUSIONS:

To the best our knowledge, evaluation of the some of these C. procera species antimicrobial activity is the first of its kind.

REFERENCES:

1. Clinical and Laboratory Standards Institute (CLSI) (2006), Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically, 7th ed.; Approved Standard M7-A7; CLSI: Wayne, PA, USA.
2. Clinical and Laboratory Standards Institute (CLSI) (1997), Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts; Approved Standard–Second Edition; M27-A2; CLSI:Wayne, PA, USA.
3. Gokturk RS (2012). In:Bitkileri Listesi (Damarlı Bitkiler). Nezahat Gokyigit Botanik Bahcesi ve Flora Aras. Der. Yayini. İstanbul.
4. Ozgen U, Kaya Y, Houghton P (2012). Turkish Journal of Biology, 36: 93-106.
5. Top H, Boke Sarıkahya N, Nalbantsoy A, Kırmızıgul A (2017). Phytochemistry, 137: 139-147.

P-089: POTENTIAL THERAPEUTIC USAGE IN NEURODEGENERATIVE DISEASES OF CEPHALARIA PROCERA FISCH. & AVÉ-LALL. IN TURKEY

[1] Yazici Bektas, N., [2] Barut, B., [3] Yesil, Y.

[1] Istanbul University, Faculty of Pharmacy, Department of Pharmacognosy, Istanbul, Turkey

[2] Karadeniz Technical University, Faculty of Pharmacy, Department of Biochemistry, Trabzon, Turkey

[3] Istanbul University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Istanbul, Turkey

INTRODUCTION:

The genus Cephalaria is one of the largest genus in family Caprifoliaceae with 94 species, it is widespread, mainly in the Mediterranean region and the Middle East. Cephalaria is represented by 39 species in Turkey (2). Some Cephalaria species are used medicinally such as Cephalaria procera Fisch. & Avé-Lall in Turkey. It is known as Ganteper, Gulinga and Cevrük, its stems are traditionally used for wound healing and antihemorhagic in Turkey (1, 4). The scope of this work was to investigate biological properties of C. procera exracts to determine its potential therapeutic usage in neurodegenerative diseases.

MATERIALS AND METHODS:

The plant materials were collected from Erzurum in July 2017. Methanol, water, n-buthanol and n-hexane extracts of C. Procera aerial parts were prepared (3). Antioxidant activities (2,2-diphenyl-1-picrylhydrazyl, phosphomolibdenum-reducing antioxidant power assays), acetylcholinesterase , butyrylcholinesterase and tyrosinase inhibitory properties of these extracts were determined according to literature (5).

RESULTS:

Methanol and water extracts showed the highest radical scavenging activities with SC50 values of 83.21 ± 3.20 and 89.91 ± 0.13 µg/mL, respectively among the tested extracts. All of extracts demonstrated the lowest reducing power activities all of concentrations when compared to quercetin. N-buthanol extract had the highest cholinesterase inhibitory properties with IC50 values of 134.63 ± 4.49 and 62.76 ± 0.63 µg/mL. In addition, n-buthanol extract (51.95 ± 0.35 µg/mL) and methanol extract (56.13 ± 1.17 µg/mL) showed higher inhibitory effects against Tyr than kojic acid (58.26 ± 0.25 µg/mL) as a positive control.

CONCLUSIONS:

Our results demonstrated that C. procera exracts would be a potential therapeutic agent for the neurodegenerative treatment.

REFERENCES:

1. Alpaslan Z (2012). Ergan Dağı (Erzincan)'nin Etnobotanik Özellikleri, Erzincan Üniversitesi Fen Bilimleri Enstitüsü, Biyoloji Anabilim Dali, Yüksek Lisans Tezi, Erzincan.
2. Gokturk RS (2012). In: Güner A, Aslan S, Ekim T, Vural M, Babaç MT (eds.). In:Turkiye Bitkileri Listesi (Damarlı Bitkiler). Nezahat Gokyigit Botanik Bahçesi ve Flora Aras. Der. Yayını. İstanbul.
3. Kayce P, Boke Sarıkahya N, Kırmızıgül S (2014). Phytochemistry Letters, 10: 324-329.
4. Ozgen U, Kaya Y, Houghton P (2012). Turkish Journal of Biology, 36: 93-106.
5. Renda G, Özel A, Barut B, Korkmaz B, Yaylı N (2018). Turkish Journal of Pharmaceutical Science.

P-090: ANTIPLATELET ACTIVITY OF LIGNANS FROM TAXUS BACCATA

[1] Kucukboyaci, N., [2] Ozkan, Y., [2] Olgac, S., [1] Sener, B.

[1]Gazi University, Department of Pharmacognosy, Ankara, Turkey

[2]Gazi University, Department of Biochemistry, Ankara, Turkey

INTRODUCTION:

Taxus baccata L. (Taxaceae), the single representative in the flora of Turkey, is an evergreen and widespread shrub commonly cultivated as an ornamental in gardens (1). Until now, the isolation of a great number of secondary metabolites, majorly taxoids as well as lignans, flavonoids, steroids, and sugar derivatives has been reported from genus Taxus. Our phytochemical investigations of T. baccata using chromatographic methods have led to the isolation of the lignans; lariciresinol (1), taxiresinol (2), 3'-demethylisolariciresinol-9'-hydroxyisopropylether (3), isolariciresinol (4), and 3-demethylisolariciresinol (5) as well as taxoids. These lignans (1-5) have evaluated for their several biological activities such as anti-inflammatory, antinociceptive, anti-ulcerogenic, antimicrobial, cytotoxic, and antioxidant as well as acetylcholinesterase, butyrylcholinesterase and lipoxygenase inhibitory activities (2,3). In continuation of our studies on screening of Turkish medicinal plants and their secondary metabolites for various biological activity to be explore as potential leading compounds, we have now evaluated the lignans (1-5) obtained from T. baccata for their antiplatelet activity.

MATERIALS AND METHODS:

Platelet aggregation was determined by in vitro turbidimetric method using an aggregometer (4). Antiplatelet activities of isolated lignans from the woods of T. baccata against platelet aggregation

induced by collagen at 1 mM and 200 µM were evaluated and compared with those of aspirin. Inhibition of platelet aggregation was expressed as percentage of inhibition in triplicate experiments.

RESULTS:

All investigated lignans, except 4, were showed inhibitory activity on platelet aggregation induced by collagen at a concentration of 1 mM with a range from 87.62±2.07 to 94.79±2.29. Otherwise, 1, 3 and 5 were exerted a low inhibition on platelet aggregation at 200 µM with inhibiton % of 11.43±1.79, 13.41±3.07 and 12.37±7.14, respectively.

CONCLUSIONS:

Our results considered that lignans from T. baccata might be investigate other platelet aggregation agonists such as arachidonic acid, thrombin and ADP to evaluate their antiplatelet activity.

REFERENCES:

1. Davis PH, Cullen J (1965). Taxus L. In: Flora of Turkey and the East Aegean Islands (Davis PH, Ed.), Vol.1, Edinburgh University Press, Edinburgh, pp. 565.
2. Kucukboyaci N, Sener B (2010). Journal of Medicinal Plants Research, 4(12): 1136-1140.
3. Kucukboyaci N, Orhan I, Sener B, Nawaz SA, Choudhary MI (2010). Zeitschrift für Naturforschung C, 65c: 187-194.
4. Born G, Cross M (1963). Journal of Physiology 168: 178-195.

P-091: ANTIPLATELET ACTIVITY OF SOME FLAVONOLS FROM SALSOLA GRANDIS AERIAL PARTS

[1] Kucukboyaci, N., [2] Calis, I., [3] Ozkan, Y., [3] Olgac, S.

[1]Gazi University, Department of Pharmacognosy, Ankara, Turkey

[2]Near East University, Department of Pharmacognosy, Nicosia, Turkish Republic of Northern Cyprus

[3]Gazi University, Department of Biochemistry, Ankara, Turkey

INTRODUCTION:

The genus Salsola L. (Chenopodiaceae) is represented by sixteen species in Turkish Flora. Among them, Salsola grandis Freitag, Vural & N. Adıgüzel, a halophytic endemic species, is narrowly distributed at Nallıhan Kuş Cenneti, Ankara (1). Salsola species have been reported to contain various bioactive constituents that have displayed several biological activities such as analgesic, anti-inflammatory, antioxidant, antihypertensive, hepatoprotective, and tyrosinase and acetylcholinesterase inhibitory activities. Our previous phytochemical studies on the aerial parts of S. grandis have led to the isolation of the flavonols and saponosides as well as one amino acid derivative compound exhibiting anti-inflammatory, antinociceptive and anticholinesterase activities. The chemical structures of the flavonols were identified as isorhamnetin-3-O-rutinoside (1), quercetin-3-O-rutinoside (2), quercetin-3-O-metyhylether (3), tiliroside (4), isorhamnetin-3-O-glucoside (5), quercetin-3-O-galactoside (6), and quercetin (7) using spectral techniques (2,3). In our continuing research on bioactive natural compounds from Turkish plants, we have now aimed to investigate antiplatelet activity of the isolated flavonols (1-7) from S. grandis in the present study.

MATERIALS AND METHODS:

Platelet aggregation was measured by using an aggregometer according to the turbidimetric method described by Born et al. (4). Antiplatelet activities of isolated compounds from the aerial parts of S. grandis against platelet aggregation induced by collagen at 1 mM and 200 µM were evaluated and compared with those of aspirin. Inhibition of platelet aggregation was expressed as percentage of inhibition in triplicate experiments.

RESULTS:

All flavonols were found effective in inhibiting platelet aggregation induced by collagen with % inhibitions ranging from 19.54±1.43 to 97.25±1.9 at a concentration of 1 mM. Among the isolated flavonols, only compound 7 exerted a notable inhibition of 61.45±12.09 at 200 µM, while compound 2 and 5 displayed a low inhibition (4.20±4.94 and 18.94±3.64).

CONCLUSIONS:

The data indicated that quercetin (7) have powerful antiplatelet activity among investigated flavonol derivatives from S. grandis.

REFERENCES:

1. Freitag H (2000). Salsola L. In: Güner A, Özhatay N, Ekim T, Başer KHC (Eds.), Flora of Turkey and the East Aegean Islands, Vol. 11, Edinburgh University Press, Edinburgh, pp. 62.
2. Kucukboyaci N, Kupeli Akkol E, Suntar I, Calis I (2016). Records of Natural Products, 10(3): 369-379.
3. Erdogan Orhan I, Kucukboyaci N, Calis I, Cerón-Carrasco JP, Den-Haan H, Peña García J, Pérez Sánchez H (2017). Phytochemistry Letters, 20: 373-378.
4. Born G, Cross M (1963). Journal of Physiology 168: 178-195.

P-092: ISOLATION OF SECONDARY METABOLITES FROM MARINE FUNGI TRICHODERMA SATURNISPORUM

[1] Demir, O., [2] Gozcelioglu, B., [1] Konuklugil, B.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

[2]The Scientific and Technological Research Council of Turkey (TUBITAK), Ankara, Turkey

INTRODUCTION:

Marine sources are known to produce structurally unique pharmaceutically potent secondary metabolites. In the past few decades, scientists have realized the importance of marine macro- and microorganisms as rich sources of new structural classes of secondary metabolites (1). Many fungi and bacteria were found to inhabit the intercellular spaces of marine macroorganisms, including marine plants as algae and sea grasses, and marine invertebrate animals as sponges and corals. Because many of these marine microorganisms have grown in unique and extreme environments, they can produce a wide variety of unusual secondary metabolites (2). The aim of this study was investigation on secondary metabolites from promising marine fungi Trichoderma saturnisporum.

MATERIALS AND METHODS:

Samples of sponge were collected from west coast of Turkey. Marine fungi were isolated from this host sponge. After the fungi were purified, identification of the fungal strains was achieved by DNA amplification. Small scale fermentation on rice and in liquid medium used for screening purposes. The chemical screening was mainly done by TLC, using different spray re-agents and by HPLC. According to the screening results, rice medium was chosen for large- scale fermentation. Three weeks later, culture medium was extracted with ethyl acetate. This extract fractionated by using VLC to yield eleven fractions. And different chromatographic techniques (CC, HPLC, TLC etc.) were performed to get pure compounds. Structure elucidation of pure compounds was done by Nuclear Magnetic Resonance Spectroscopy.

RESULTS:

Four compounds were isolated. First compound is 2-methyl 2,5,7 nonatriene 4- one and third compound is 3,5- di hydroxyl benzene acetic acid methyl ester. For the second compound main structure was determined but because of the quantity deficiency alkyl groups couldn't be determined. Fourth compound is a mixture of two sterols and one of these sterols has been determined as ergosterol.

CONCLUSIONS:

This is the first report on isolation and characterization of bioactive compounds of marine derived fungus in Turkey.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (114S916)

REFERENCES:

1. Bacon CW, White JF (2000). Microbial Endophytes. Marcel Deker Inc., New York.
2. Liming J, Chunshan Q, Xiyan H, Shengdi F (2016). Marine Drugs 14:76

P-093: ANTIMICROBIAL ACTIVITY OF ENDOPHYTIC FUNGI FROM PANCRATIUM MARITIMUM L.

[1] Ozcinar, O., [2] Ozturk, I., [3] Ermertcan, S., [1] Kivcak, B.

[1]Ege University, Faculty of Pharmacy, Department of Pharmacognosy, Izmir, Turkey

[2]Izmir Katip Celebi University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, İzmir, Turkey

[3]Ege University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Izmir, Turkey

INTRODUCTION:

Endophytes, spends whole/part of its life cycle inside the healthy tissues of the host plant within a mutual benefit relationship, and do not cause apparent disease symptoms. In recent years they are one of the most compelling group of microorganism due to the contiously interaction with the host plant and other microorganisms. Also they are promising source of new bioactive secondary metabolites (1). Pancratium maritiumum L. (Amaryllidaceae) is distributed in the Mediterranean, the Atlantic, the Black and Caspian coasts and has attracted attention due to its alkaloid content with significant therapeutic properties (2). The aim of this study is to investigate the antimicrobial activities of the endophytic fungi of P. maritimum.

MATERIALS AND METHODS:

Ethylacetate extracts of the fermentation brothsof endophytic fungi, Talaromyces cellulolyticus (1), Penicillium chrysogenum (2), Chaetomium globosum (3), Fusarium solani (4) and co-culture (5) of 1 and 4 tested for antimicrobial activity against Staphylococcus aureus ATCC 29213, Enterococcus faecalis ATCC 29212, Escherichia coli ATCC 25922, Pseudomonas aeruginosa ATCC 27953 and Candida albicans ATCC 90026 strains. Inhibitory effects of the extracts were examined by disc diffusion method by determining of inhibition zone diameters. Minimum inhibitory concentrations (MIC) of the extracts were also determined by microdilution method.

RESULTS:

As a result of disc diffusion method 2 exhibited antimicrobial activity to all strains. Moreover C. albicans and E. faecalis were also inhibited only by 2

at studied concentrations. Except 1 all of the extracts were active againts E. coli. Extracts of 3 and 5 showed activity againts S. aureus and E. coli, 4 and 5 showed activity againts P. aeruginosa. MICs of the extracts against bacteria and yeast were shown in Table 1.

Table 1. MICs of the extracts against bacteria and yeast (µg/ml)

Microorganisms		Extracts						Control	
		1	2	3	4	5	K	CIP	FLU
Gram-positive	S. aureus	>4096	64	1024	1024	256	-	0.125	-
	E. faecalis	>4096	256	>4096	>4096	>4096	-	0.5	-
Gram-negative	E. coli	>4096	128	1024	1024	1024	-	0.004	-
	P. aeruginosa	>4096	256	>4096	>4096	>4096	-	0.5	-
Yeast	C. albicans	512	64	256	1024	512	-	-	1

(-): No inhibitory effect, CIP:Ciprofloxacin, Flu: Fluconazole, K: EtOAc extract of broth medium

CONCLUSIONS:

This study showed potent antibiotic activity of endophytic fungi from P. maritimum. As far as can be ascertained from the literature this is the first endophytic fungi isolation study of P. maritimum. Bioactivity- guided isolation and purification study of these endophytes is planned for further studies.

REFERENCES:

1. Aly AH, Debbab A, Proksch P (2013). Pharmazie 68: 499-505.
2. Cedron JC et al., (2009). Journal of Natural Products72: 112-116.

P-094: COMPOUNDS FROM AERIAL PARTS OF SCORZONERA TOMENTOSA

Bahadir Acikara, O., Ozbilgin, S., Ergene Oz, B., Kurtul, E., Saltan Iscan, G.

Ankara University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

Scorzonera tomentosa L., belonging to Asteraceae family is an endemic species to Turkey (1). In Turkish folk medicine this plant roots and latex obtained from the roots are used for treatment of wounds (2). Current study is aimed to investigate phytochemical content of the S. tomentosa aerial parts.

MATERIALS AND METHODS:

Aerial parts of the S. tomentosa (AEF No: 23841) were dried, powdered and macerated in methanol at room temperature. The extract was filtered and evaporated until dryness under reduced pressure at 50°C. The crude extract was subjected to liquid partitioning yielding the fractions of petroleum ether, chloroform, ethylacetate and water. Separation was carried out from an aqueous extract on C18 column chromatography by eluting with water:methanol mixture in different ratio; from 90:10 to 0:100. Obtained fractions (210 fractions) from the column were combined according to the TLC and HPLC profiles. Different chromatographic methods such as column chromatography on Silicagel, sephadex LH-20, preparative TLC, preparative HPLC were used for isolation and purification of the compounds from fractions. Structure elucidation of the compounds were performed by using spectroscobic techniques (1H, 13C and 2D-NMR, MS).

RESULTS:

Chlorogenic acid, hydrangenol-8-O-glucoside, cichoriin, 7-O-methyl isoorientin, isoorientin, swertisin, 7-methoxy apigenin-6-C-apiofuranosyl-(1‴ → 2″) glucoside and apigenin-6-C-apiofuranosyl-(1‴ → 2″) glucoside were obtained from water fraction of the methanolic extract.

CONCLUSIONS:

In the current study, S. tomentosa aerial parts have been investigated for its chemical content for the first time. Results have revealed that aerial parts contain flavonoids mainly.

ACKNOWLEDGEMENTS:

This study was supported by Ankara University (BAP) Project No: 13B3336003.

REFERENCES:

1. Davis PH (1975). Flora of Turkey and the East Aegean Islands, vol. 5, University, Press, United Kingdom, pp 632–657.
2. Sezik E. et al., (1997). Economic Botany, 51: 195-211.

P-095: ENZYME INHIBITORY EFFECT OF TWO SIDERITIS SPECIES ENDEMIC TO TURKEY

[1] Ceylan, R., [1] Zengin, G., [1] Aktumsek, A.

[1] Selcuk University, Faculty of Science, Department of Biology, Konya, Turkey

INTRODUCTION:

The genus Sideritis comprises more than 150 species distributed in the temperature and tropical regions of Northern Hemisphere especially in the Mediterranean basin (1). Sideritis species have been traditionally used as teas and therapeutics (1). The aim of this study, was to explore the methanol extracts of two Sideritis (Sideritis arguta Boiss Et Heldr and Sideritis bilgerana P. H. Davis) for their bioactive compounds and enzyme inhibitory effects.

MATERIALS AND METHODS:

We investigated enzyme inhibitory properties of the methanol extracts of S. arguta and S. bilgerana against cholinesterase (AChE and BChE), tyrosinase, amylase and glucosidase as well as total phenolic and flavonoid contents via colorimetric methods.

RESULTS:

S. arguta extract exhibited higher cholinesterase abilities (4.23 mgGALAE/g for AChE and 2.35 mgGALAE/g for BChE) than S. bilgerana extract (3.86 mgGALAE/g for AChE and 0.81 mgGALAE/g for BChE). Similar results have been founded for the other enzymes (tyrosinase, amylase, glucosidase). However, S. arguta showed lower total phenolic and flavonoid contens (112. 21 mgGAE/g and 31.03 mgRE/g, respectively) in comparison with S. bilgerana (117.23 mgGAE/g and 51. 78 mgRE/g, respectively).

CONCLUSIONS:

On the basis of our results, S. arguta and S. bilgerana methanol extracts might be considered as a potential source of natural enzyme inhibitors in food, medicinal, and pharmacological areas.

REFERENCES:

1. Gonzalez-Burgos E, Carretero ME, Gomez-Serranillos MP (2011). Journal of Ethnopharmacology, 135: 209-25.

P-096: CHOLINESTERASE INHIBITION AND ANTIOXIDANT PROPERTIES OF ONOSMA SERICEA AND ONOSMA STENOLOBA METHANOL EXTRACTS

[1] Zengin, G., [1] Ceylan, R., [2] Katanić, J., [1] Aktumsek, A.

[1] Selcuk University, Faculty of Science, Department of Biology, Konya, Turkey

[2] University of Kragujevac, Faculty of Science, Department of Chemistry, Kragujevac, Serbia

INTRODUCTION:

Onosma species (Boraginaceae) widely distributed in Turkey. Several Onosma species are used as folk medicine (1). The focus of this research was the antioxidant potential and cholinesterase enzymes inhibitory effect of the Onosma sericea Willd and Onosma stenoloba Hausskn. ex Riedl.

MATERIALS AND METHODS:

In this study, antioxidant capacities (DPPH and ABTS radical scavenging, CUPRAC and FRAP, phosphomolibdenum assay, and metal chelating activity) and cholinesterase enzymes (Acetylcholinesterase:AChE and Butyrlcholinesterase:BChE) inhibition prorperties of O. sericea and O. stenoloba methanol extracts were investigated with colorimetric methods.

RESULTS:

O. sericea extract showed higher antioxidant activity on DPPH and ABTS radicals (170.23 mg TE/g and 235.53 mg TE/g, respectively) in comparison with O. stenoloba (53.96 mgTE/g and 95.60 mg TE/g, respectively). Similar pattern was observed for the other antioxidant tests, including CUPRAC and FRAP assays, phosphomolybdenum assay, and metal chelating activity. However, O. sericea extract demonstrated lower cholinesterase inhibitory abilities (both AChE and BChE) than O. stenoloba extract.

CONCLUSIONS:

According to our results, O. sericea and O. stenoloba extracts may be considered as a valuable source of natural antioxidants and cholinesterase inhibitors for discovering novel functional products, such as pharmaceutical preparations and nutraceuticals.

ACKNOWLEDGEMENTS:

This work was supported by Ministry of Education, Science and Technological Development, Republic of Serbia, Grant No. III43004.

REFERENCES:

1. Ozgen O, Houghton PJ, Ogundipe Y, Coskun M (2003). Fitoterapia, 74: 682- 685.

P-097: ANTIOXIDANT ACTIVITY OF TARAXACUM MIRABILE WAGENITZ AERIAL PARTS, AS AN ENDEMIC SPECIES OF TURKEY

[1,2] Karahuseyin, S., [3] Ozsoy, N., [1] Sari, A.

[1]Istanbul University, Faculty of Pharmacy, Department of Pharmacognosy, Istanbul, Turkey

[2]Cukurova University, Faculty of Pharmacy, Department of Pharmacognosy, Adana, Turkey

[3]Istanbul University, Faculty of Pharmacy, Department of Biochemistry, Istanbul, Turkey

INTRODUCTION:

The genus Taraxacum is a member of the family Asteraceae, subfamily Cichorioideae, tribe Lactuceae. Taraxacum species are cosmopolite plants and have long been used traditionally in folk medicine for its curative properties such as dyspepsia, heartburn, spleen and liver complaints, anorexia, diabetes, cancer and gastric, renal and hepatic ailments [1, 2]. Taraxacum mirabile Wagenitz is an endemic species to Turkey and grows in the central part of the country. In this study, the antioxidant activity of ethyl acetate, buthanol, dichloromethane and petroleum ether fractions of the ethanol extract from the aerial parts of T. mirabile Wagenitz were investigated.

MATERIALS AND METHODS:

Antioxidant activity was assayed by 6 different methods including the total phenols assay by Folin-Ciocalteu reagent (FCR), ferric ion reducing antioxidant power (FRAP), DPPH free radical and thiobarbituric acid test using the lipid peroxidation of liposomes. Total flavonoid content was determined by using a colorimetric method [3]. Antioxidant activities exhibited by the extracts evaluated by these assays reflect the capacity of the extracts to act as electron or hydrogen atom donors, a necessary requirement for antioxidant function in biological systems.

RESULTS:

It was found that the extracts are able to scavenge DPPH, ABTS radicals, and reduce Fe3+ to Fe2+ in the ferric reducing antioxidant power (FRAP) assay. Ethyl acetate (including 49.53 mg/g total phenolic compounds) and dichloromethane extracts (45.03 mg/g) from the aerial parts of the plant showed the highest antioxidant activity due to their richest phenolic contents, followed by buthanol extracts (26.93 mg/g), whereas, petroleum ether extracts (15.97 mg/g) containing the least phenolics, were weakest in activity.

Conclusion: We found that ethyl acetate extract from aerial parts of T. mirabile Wagenitz is an alternative source of phenolic compounds, which may contribute to the overall antioxidant activity of the extracts.

REFERENCES:

1. Schütz K et al., (2006). Journal of Ethnopharmacology, 107: 313 – 323.
2. Martinez M et al., (2015). Journal of Ethnopharmacology, 169: 244-262.
3. Sakanaka S et al., (2005). Food Chemistry, 89 (4): 569-575.

P-098: PHYTOCHEMICAL STUDIES ON ACANTHUS DIOSCORIDIS L. VAR. DIOSCORIDIS

[1] Sarikaya Aydin, S., [2] Duez, P., [3] Harput, U.S., [1] Saracoglu, I.

[1]Hacettepe University, Department of Pharmacognosy, Ankara, Turkey

[2]Mons University, Laboratory of Therapeutic Chemistry and Pharmacognosy, Mons, Belgium

[3]Hacettepe University, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

The genus Acanthus L. (Acanthaceae), represented by five species in Turkish flora, is important traditional Turkish medicine and a series of biological activity such as antioxidant, hepatoprotective, antitumor and anti-carsinogenic effects were reported for some species from genus Acanthus. The chemical constituents isolated from Acanthus sp. include alkaloids and glycosides of lignans, benzoxazinoids, megastigmanes, phenylethanoids, flavones and aliphatic alcohols (1). Acanthus dioscoridis L. (Bear's breeches) and Acanthus hirsutus Boiss leaves decoction is used in Eastern Anatolia for wound healing, expectorant and antidiarrheal effects (2).

Materials and Methods The aqueous extract was subjected to polyamide column chromatography.

RESULTS:

Repeated column chromatographies of polyamide column fractions resulted in the isolation of three known phenylethanoid glycosides.

CONCLUSIONS:

The structures of the compounds were identified as martynoside, leucoceptoside A and acteoside on the basis of spectroscopic (1D/2D NMR and FAB-MS) data.

ACKNOWLEDGEMENTS:

This study was supported by TUBITAK (2211-C) and TUBITAK (2214-A).

REFERENCES:

1. Harput US, Arihan O, Iskit AB, Nagatsu A, Saracoglu I (2011). J Med Food, 14 (7/8): 767–774.
2. Baytop T (1999). Türkiye'de Bitkilerle Tedavi (Geçmişte ve Bugün). İstanbul, Nobel Tıp Kitabevleri Ltd. Şti.

P-099: ISOLATION OF POTENT LIVER X RECEPTOR AGONIST COMPOUNDS FROM HYPERICUM MICROCALYCINUM BOISS. & HELDR.

[1] Sarikaya Aydin, S., [1] Kutluay, V.M., [2,3] Bai, F., [2] Makino, T., [4] Harput, U.S., [1] Saracoglu, I.

[1]Hacettepe University, Department of Pharmacognosy, Ankara, Turkey

[2]Nagoya City University, Department of Pharmacognosy, Nagoya, Japan

[3]The Kochi Prefectural Makino Botanical Garden, Kochi, Japan

4Hacettepe University, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

The genus Hypericum L. (Hypericaceae) is represented by 100 taxa grouped under 19 sections 45 of which are endemic in Turkey. Hypericum species are used as antispasmodic, sedative and antihelmintic internally; antiseptic and for wound healing externally in Anatolia (1,2). They contain naphthodianthrones, flavonoids, tannins, xanthones, essential oils.

MATERIALS AND METHODS:

Hypericum microcalcinum Boiss. & Heldr. was studied on the fractions with the highest radical scavenging effect against radicals DPPH, NO and SO, which were found to be rich in flavonoids obtained from the polyamide column by aqueous extract. The effect of this fraction on inflammatory mechanisms was investigated by luciferase reporter gene assay in terms of agonist activity in liver X receptors (3).

RESULTS:

When the aqueous extract and the LXR agonist activities of the tested fraction were examined, while there was no significant activity in the aqueous extract, there was moderate activity in the fraction and fold change was calculated to be 1,37. As a result of the phytochemical studies 6 phenolic substances were obtained from the active fraction.

CONCLUSIONS:

The structures of the isolated compounds were identified as catechin and epicatechin, apigenin-8-C-(2-O-acetyl)-glucopyranoside, quercetin-3-O-glucopyranoside, quercetin-3-O-arabinopyranoside, kaempferol-3-O-arabinopyranoside, luteolin-8-C-glucopyranoside on the basis of spectroscopic data. Apigenin-8-C-(2-O-acetyl)-glucopyranoside was isolated for the first time in Hypericum genus.

REFERENCES:

1. Robson NKB (1966). In: Davis PH (ed). Hypericum L. in. Flora of Turkey and the East Aegean Islands. Edinburg University Press, Edinburgh, UK, pp 355-401.
2. Baytop T (1999). Nobel Tıp Kitabevleri Ltd. Şti, pp 166-167.
3. Nakashima KI, Murakami T, Tanabe H, Inoue M (2014). Biochimica et Biophysica Acta, 1840: 3034-3041.

P-100: EFFECT OF POLYGONUM COGNATUM ON ALPHA-GLUCOSIDASE INHIBITORY ACTIVITY

[1] Gozcu, S., [2] Ozbek, H., [2] Guvenalp Z.

[1] Erzincan University, Faculty of Pharmacy, Department of Pharmacognosy, Erzincan, Turkey

[2] Atatürk University, Faculty of Pharmacy, Department of Pharmacognosy, Erzurum, Turkey

INTRODUCTION:

The genus Polygonum (Polygonaceae) is represented by 40 species and 6 subspecies in Turkish flora (1,2). Polygonum cognatum Meissn. is one of these species and known as madımak and çoban ekmeği in Anatolia. Its leaves are used in Turkish folk medicine as antidiabetic and diuretic (3). It is reported that quercetin-3-glycoside, quercetin-3-rutinoside, quercetin-3-methylether, kaempferol-3-methylether, kaempferol-3-glycoside, β-sitosterol, p-hydroxybenzoic acid, vanillic acid, gallic acid and protocatechuic acid were purified from the leaves of P. cognatum (4). The aim of this study is to evaluate the α-glucosidase inhibitory activity of herba from P. cognatum.

MATERIALS AND METHODS:

In the present study, the methanol extract from herba of P. cognatum and its different polarity fractions (petroleum ether, dichloromethane, ethyl acetate, n-butanol) were evaluated for in vitro α-glucosidase inhibitory activities according to the method of Tao et al., 2013 (5).

RESULTS:

The ethyl acetate fraction showed the best α-glucosidase inhibitory activity with 85.59% (IC50=0.0097mg/ml) when compared with the standard compound acarbose that displayed 2.21% inhibitory activity (IC50=3.5148 mg/ml) at 50 µg/ml concentration. The methanol, n-butanol, hexane and dichloromethane extracts showed 55.47% (IC50=0.0463 mg/ml), 51.43% (IC50=0.0478 mg/ml), 36.93% (IC50=0.0643 mg/ml) and 9.29% (IC50=1.3158 mg/ml) inhibition activity at the same concentration, respectively.

CONCLUSIONS:

These results indicate that the ethyl acetate extract has a high potential for α-glucosidase inhibitory activity.

REFERENCES:

1. Guner A, Aslan S, Ekim T, Vural M, Babaç MT (2012). In: Turkiye Bitkileri Listesi (Damarlı Bitkiler), Nezahat Gokyigit Botanik Bahcesi Yayınevi. İstanbul, pp 758-761.
2. Coode MJ, Cullen JE (1985). In: Davis PH (ed). *Polygonum* L., Flora of Turkey and the East Aegean Island,Vol.2, Edinburg University Press, UK, pp 269-281.
3. Baytop T. 1999. In: Turkiye'de Bitkiler ile Tedavi-Gecmiste ve Bugün. Nobel Tıp Kitabevleri, Türkiye, pp 233-244.
4. Ulubelen A, Tan N, Ucer M (1992). Fitoterapia, 63:87.
5. Tao Y, Zhang Y, Cheng Y, Wang Y (2013). Biomed Chromatogr, 27:148-155.

P-101: ANATOMY OF PAEONIA MASCULA (L.) MILL. (PAEONIACEAE)

[1] Gozcu, S., [2] Karakaya, S., [2] Guvenalp, Z.

[1], Erzincan University, Faculty of Pharmacy, Department of Pharmacognosy, Erzincan, Turkey

[2] Atatürk University, Faculty of Pharmacy, Department of Pharmacognosy, Erzurum, Turkey

INTRODUCTION:

The genus Paeonia (Paeoniaceae) is represented by six species and four subspecies in Turkey (1). Paeonia mascula (L.) Mill. is one of these species and known as "Gülorç, Gülhorç, Ayı gülü, Eşek gülü" in Turkey (2). The leaves of the plant are used in

Turkish folk medicine as antidiabetic, sedative and antitussive (2,3). It is reported that the aerial parts of P. mascula contain tannin, flavonoid, essential oil and alkaloids (4). The aim of this study is to investigate the anatomical structures of the stem, leaf, petiole, petal and fruit of P. mascula.

MATERIALS AND METHODS:

The plant material was collected from Aşkale/ Erzurum (Turkey) in July 2017. Specimens were dried according to standard herbarium techniques and stored in the Herbarium of Atatürk University, Faculty of Pharmacy. The materials for anatomical study were preserved in 70% alcohol. In this study, anatomical structures of the stem, leaf, petiole, petal and fruit of P. mascula were investigated. Characteristic elements of these parts of the plant were identified with taking the sections. Their structures were illustrated with photographs.

RESULTS:

The leaf is bifacial and stoma were located in the lower leaf epidermises. The unicellular trichomes and druses were observed in the leaf and stem of P. mascula. The petiole anatomy of P. mascula is similar to anatomy of the stem. Cuticula is striated. In anatomy of pericarp starch-bearing parenchyma was found. Druses were also found in the seed.

CONCLUSIONS:

In the present study, anatomical structures of the stem, leaf, petiole, petal and fruit of P. mascula were investigated. The anatomical properties given in this study provide description of P. mascula. The findings obtained in this study propose that this anatomical diversity may be beneficial in taxonomical classification.

REFERENCES:

1. Cullen JE (1985). In: Davis PH (ed). *Paeonia* L., Flora of Turkey and the East Aegean Island, Vol.1. Edinburg University Press., UK, pp 204-206.
2. Arituluk ZC, Ezer N (2012). Hacettepe Üniversitesi Eczacılık Fakültesi Dergisi, 32 (2):179-208.
3. Baytop T (1999). In: Turkiye'de Bitkiler ile Tedavi-Gecmiste ve Bugün. Nobel Tıp Kitabevleri, Türkiye, pp 233-244.
4. Sevim D, Senol, FS, Gulpinar AR, Erdogan Orhan İ, Kaya E, Kartal M, Sener B (2013). Industrial Crops and Products, 49:240-246.

P-102: DETERMINATION OF OLEUROPEIN IN OLIVE LEAVES (OLEA EUROPAEA L.) AND COMMERCIAL OLIVE LEAF EXTRACTS

[1] Isik, S., [2] Kartal, M.

[1] Near East University, Department of Analiytical Chemistry, Nicosia, TRNC

[2]Bezmi Alem Vakif University, Department of Pharmacognosy, Istanbul, Turkey

INTRODUCTION:

Olea europaea L. is the symbol of Mediterranean. Its leaf's main component is oleuropein; a polyphenol that can help lower bad cholestrol, prevent cancer and oxidative damage (1,2).Several researches showed that olive leaf extract decreases the blood pressure (3) and increases the blood flow in arteries (4).The aim of this study is to determine the oleuropein amount in olive leaf varieties of different regions of Turkey and some commercial olive leaf extracts, according the European Pharmacopoeia 6.0.(EP6.0).

MATERIALS AND METHODS:

Olive leaves collected from different regions (Kilis, Nizip Gemlik) of Turkey and North Cyprus (Nicosia). Three different commercial olive leaf extracts obtained from local markets of Turkey.All samples are extracted by according the EP6.0.

Samples were analysed with Agilent Technologies 1200 series HPLC and seperated with Eclipse XDB-C18 column(150 mmx4.6 mm,5µm). Gradient solvent system consist of (A):methanol and (B):water with 1%glacial acetic acid was used as mobile phase at a flow rate of 1 mL min-1. Detection wavelength was set at 254 nm.

RESULTS:

Oleuropein was observed in all samples (Table 1). According to the results, sample from Kilis and the commercial extract P3 has the highest oleuropein. Sample from N.Cyprus and the commercial extract P2 has the lowest oleuropein.

Table 1. Percentages of oleuropein and peak areas of oleuropein standard, olive leaf samples from different geographical regions and commercial olive leaf extracts from local markets of Turkey.

Sample	1st Analysis	2nd Analysis	3rd Analysis	Average of Peak Areas	Oleuropein (%)
Oleuropein	421	420.9	422.8	421.56 ±1.07	-
Kilis	679.9	659.6	660.8	666.76 ±11.39	6.32
Kilis 2 years old	510	510.2	510.2	510.13±0.11	4.84
Nizip	411.5	410.9	408.8	410.4±1.41	3.89
Gemlik	276.9	255.2	255.5	262.53±12.44	2.49
North Cyprus	178	179.1	177.2	178.1±0.95	1.69
P1*	767.9	760.8	756.9	761.86±5.57	7.22
P2*	322.8	323.3	323	323.03±0.25	3.06
P3*	1078.1	1074.6	1088.5	1080.4±7.23	10.25

*Commertial olive leaf extracts are coded as P1, P2 and P3.

CONCLUSIONS:

The percentages of oleuropein are varies for each sample. When compared, sample from Kilis and commercial extracts P1 and P3 are compatible with EP6.0.

REFERENCES:

1. Omar SH. (2010). Sci Pharm.78(2):133-154.
2. Wahle et al.(2004). *Lipids*.39(12):1223.
3. Samuelsson G. (1951).*Farm Revy*.15(1):229-239.
4. Zarzuelo et al. (1991) *Planta Med*.57(5):417-419.

P-103: FATTY ACID PROFILE OF SOME COMMERCIAL BLACK CUMIN (NIGELLA SATIVA L.) SEED OIL CAPSULES

[1] Isik, S.,[2] Aslan Erdem, S.,[3] Kartal, M.

[1]Near East University, Faculty of Pharmacy,,Department of Analiytical Chemistry, Nicosia, TRNC

[2]Ankara University, Faculty of Pharmacy, Department of Pharmacognosy,Ankara,Turkey

[3]Bezmi Alem Vakif University, Faculty of Pharmacy, Department of Pharmacognosy,Istanbul,Turkey

INTRODUCTION:

Black cumin is a medicinally and economically important plant. Most important component of it's essential oil is thymoquinone.Acoording to recent researches, major fatty acids of black cumin seed oils are linoleic, oleic and palmitoleic acids(1–4).

MATERIALS AND METHODS:

Seed oil capsules were supplied from local markets in Ankara. For fatty acid methyl esterification (FAME);150 mg oils were placed in 25ml of volumetric flasks, saponified by adding 4ml 0.5 N NaOH/MeOH, and heated on a steam bath until the fat globules disappeared. 4ml of BF3 /MeOH was added to each flask and were boiled for 2 minutes.After the solutions were cooled down at room temperature, they were filled upto 25ml with saturated sodium chloride solution. The obtained FAMEs were dissolved in 2ml n-hexane and 1µl of samples was injected and analyzed by GC-MS.Chromatographic analysis was carried out on Agilent 6890N Network GC system combined with Agilent 5973 Network MS Detector (GC-MS). The capillary column used was HP Innowax Capillar y;60.0m ×0.25mm×0.25µm.Helium was used as carrier gas (5).

RESULTS:

Fatty acid profiles were given in Table1. Major fatty acids (linoleic, oleic and palmitic acids) were observed in all samples. According to the given table below, Samples 8, 7 and 6 has the highest linoleic, oleic and palmitic acid respectively.

Table 1. Fatty acid profiles of black cumin oil capsules

Fatty Acids	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6	Sample 7	Sample 8	Sample 9	Sample 10
C14:0	0.13	-	-	0.08	0.137	0.164	0.073	-	0.128	0.13
C16:0	11.349	8.893	12.04	7.90	11.285	12.716	10.665	8.345	12.345	11.996
C16:1	-	-	-	-	-	0.159	0.136	-	0.174	-
C18:0	3.901	3.144	3.53	3.98	3.893	3.660	5.425	3.906	3.878	3.934
C18:1	27.384	46.712	24.93	34.35	27.349	26.396	35.082	31.132	26.346	27.198
C18:2	50.610	36.677	56.45	52.84	50.31	53.845	45.154	56.616	54.389	53.632
C18:3	0.594	2.945	-	-	0.625	-	1.685	-	-	-
C20:0	-	-	-	-	-	-	0.521	-	-	-
C20:1	1.141	-	-	-	1.234	-	-	-	-	-
C20:2	2.737	1.629	3.05	0.85	2.691	2.760	1.258	-	2.74	3.109
C22:2	2.154	-	-	-	2.475	-	-	-	-	-

CONCLUSIONS:

The percentages of fatty acids are varies of each samples. Major fatty acid amouts are compatible with other researches.

REFERENCES:

1. Kaskoos RA (2011). Res J Med Plant, 5(1):85-89.
2. Lutterodt et al., (2010). LWT-Food Sci Technol. 43(9):1409-1413.
3. Ramadan et al., (2002). Nahrung-Food, 46:2-
4. Tulukcu E., (2011). African J Agric Res, 6(4):892-895.
5. Uğur et al., (2010). Pharmacogn Mag, 6(24):305.

P-104: ANTIOXIDANT AND ANTIMICROBIAL EFFECTS OF EXTRACTS PREPARED FROM ANTHEMIS TINCTORIA VAR. TINCTORIA

[1] Tufan, S., [2] Taşkin, T., [3] .Tuysuz, M.,[1] Mat, A.

[1]Istanbul University, Department of Pharmacognosy, Istanbul,Turkey

[2]Marmara University, Department of. Pharmacognosy, Istanbul, Turkey

[3]Istanbul University, Department of Microbiology, Istanbul, Turkey

INTRODUCTION:

The genus Anthemis, represented by 81 taxa, 51 species including 29 endemic in Turkey, has various applications in Turkish folk medicine (1). In present study, antimicrobial and antioxidant properties of A. tinctoria var. tinctoria aerial parts have been investigated.

MATERIALS AND METHODS:

Maceration method was used in order to obtain sesquiterpenes and phenolic compound extracts. The antimicrobial activity of the dichloromethane extracts was determined by the microbrothdilutions technique using the Clinical Laboratory Standards Institute (CLSI) recommendations (2, 3). Antioxidant properties of methanol and %80 aqueus methanol extracts were determined in terms of total phenolic contents, DPPH radical scavenging activity, Ferric reducing/antioxidant power (FRAP) assay, Cupric reducing antioxidant capacity (CUPRAC) assay(4).

RESULTS:

All of the dicholoromethane extracts showed antimicrobial activity at 1250 µg/ml against S. epidermidis and E. faecalis. Extracts were more effective against gram positive bacteria, except S. aureus and none of them has potential against gram negative bacteria and C. albicans. Methanol and 80% aqueous methanol extracts, especially methanol extract coded ATVT2 (DPPH; %83.45±0.2,at 200

µg/mL, FRAP assay; 0.247±0.006 mM Fe2+/mg extract, CUPRAC;b1.250±0.001 and Total phenolic; 100±0.009 mgGAE/g extract) had promising antioxidant activity,

CONCLUSIONS:

According to the results phenolic extracts, or isolated components, obtained from A. tinctoria var. tinctoria might serve as preventive agents in the future. Further studies are currently in progress.

REFERENCES:

1. Uzel A et al., (2004). Journal of Ethnopharmacology, 95:151–154.
2. Clinical and Laboratory Standards Institute (CLSI), Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically. Approved Standard 7th Edition, M7-A7, Wayne, PA, USA, 2006.
3. Clinical and Laboratory Standards Institute (CLSI), Reference method for broth dilution antifungal susceptibility testing of yeasts. Approved Standard 3th Edition. M27-A3. Wayne, PA, USA, 2008.
4. Ozsoy N et al., (2008). Food Chemistry 110(3): 571-83.

P-105: COMPARISON OF THE VOLATILE COMPOSITION OF SOME FENNEL HERBAL TEAS (FOENICULUM VULGARE MILL.) FROM TURKEY

[1] Sabanoglu, S.,[1] Karacaoglu, M., [2] Kilic, E., [1] Aslan Erdem, S.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

[2]Ankara University Development Foundation Private Anatolian High School, Ankara, Turkey

INTRODUCTION:

Herbal teas are commonly consumed beverage due to their therapeutic and healing properties for worldwide. The popularity of herbal teas associates with their high availability, the low prices, and the minimal side effects (1). Foeniculum vulgare (Apiaceae), commonly known as fennel, is a well-known and commercially important medicinal and aromatic plant. Its fruits are widely used as carminative, digestive, galactagogue and diuretic and in treating respiratory and gastrointestinal disorders (2, 3). The functional properties of fennel, are commonly used, are mainly derived from their volatile oil. Consequently, our study concentrated on a comparison of the volatile composition of some fennel herbal teas from Turkey.

MATERIALS AND METHODS:

For this study, three herbal fennel tea were purchased from a major supermarket and coded as Fennel 1–3. Contents of the herbal fennel tea were subjected to water distillation with a Clevenger apparatus for 4 hours. The essential oil samples were analyzed by GC–MS using the Agilent 6890N Network GC system combined with an Agilent 5973 Network mass selective detector.

RESULTS:

In this study, components were identified in the oil. The main components of the essential oils were found as anethole, carvone, carvacrol, estragole, limonene, anisaldehyde, α-fenchone. Anethole was the major component of the essential oils (Fennel-1 (85.43%), Fennel-2 (89.08%) and Fennel 3 (93.22%)).

CONCLUSIONS:

GC-MS results are in agreement with the current literature and there commended limit in Turkish Pharmacopoeia 2016 for anethole, estragole, α-fenchone. According to the pharmacopoeia, the fennel essential oil must contain at least 80% anethole (2, 3).

REFERENCES:

1. Pohl P, Dzimitrowicz A, Jedryczko D, Szymczycha-Madeja A, Welna M, Jamroz P (2016). Journal of Pharmaceutical and Biomedical Analysis, 130: 326-335.
2. Kan Y, Kartal M, Aslan S, Yildirim N (2006). Journal of Faculty of Pharmacy of Ankara University, 35: 95-101.
3. Rather MA, Dar BA, Sofi SN, Bhat BA,Qurishi MA (2016). Arabian Journal of Chemistry, 9: 1574-1583.

P-106: ESSENTIAL OIL COMPOSITION OF ACHILLEA COARCTATA POIR

Sabanoglu, S., Aslan Erdem, S., Altun, M.L.

Ankara University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

The genus *Achillea* belongs to the Asteraceae family, comprises more than 100 species throughout the world, mainly distributed in Northern hemisphere as a mythological plant. The genus is represented by 47 species and 24 of them are endemic in Turkey(1).*Achillea* species have several components such as essential oils, phenolic acids, flavonoids, terpenes, lignans. *Achillea* species have been used in traditional medicine as antimicrobial, antioxidant, antispasmodic, estrogenic, antiulcer agents. In this study, essential oil composition of *Achillea coarctata* Poir. was investigated.

MATERIALS AND METHODS:

Aerial parts of A. coarctata were collected near Develi-Kayseri in their flowering stage (2016). The air-dried and milled inflorescences and leaves of plant were hydrodistilled for 3 h using a Clevenger-type apparatus. The oils were analyzed by GC/MS and the components of essential oils were identified by comparison of retention times and their mass spectra

to those from MS library.

RESULTS:

The amount of oil calculated per weight of the dried plant was (v/w) 0.12%. Thirty-two components were identified representing approximately 96.0% of the total oil. 1,8-cineol (17%), viridiflorol (13%), borneol (7%) and camphor (6%) were found as the main components of the essential of A. coarctata.

CONCLUSIONS:

The essential oil composition of A. coarctata has been reported in previous studies. 1,8-cineol (20%), camphor (16%) and viridiflorol (12%) were found to be the major components by Toker et al. (2) while, viridiflorol (26%), camphor (10%) and caryophyllene oxide (10%) were reported as main components by Turkmenoglu et al. (3). Comparing the previous data with this study, it becomes evident that viridiflorol and camphor are one of the major components of A. coarctata in both studies.

REFERENCES:

1. Rahimmalek M, Tabatabaei BES, Arzani A, Etemadi N (2009). Biochemical Systematics and Ecology, 17: 354-361.
2. Toker Z, Ozen HC, Clery RA, Owen NE (2003). Journal of Essentia Oil Research, 15: 100-101.
3. Turkmenoglu FP, Agar OT, Akaydin G, Hayran M, Demirci B (2015). Molecules, 20: 11432-11458.

P-107: THE ESSENTIAL OIL CONTENT OF SOME ENDEMIC PEUCEDANUM SPECIES

[1] Arabaci Anul, S., [2] Aslan Erdem, S.,[3] Coskun, M.

[1]The Ministry of Health of Turkey, Medicines and Medical Devices Agency, Ankara, Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

[3]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

INTRODUCTION:

Peucedanum species have medical uses primarily in traditional Chinese medicine, Japan, Iran, Bulgaria and Turkey. Some species are well-known herbal drugs in Chinese medicine and listed in the Chinese Pharmacopoeia (1). In Turkey, there are 21 species, 9 of them are endemic and they are also used as a therapeutic and protective agent. (2-3). Recent studies have shown that Peucedanum species have several bioactive substances, including coumarins and essential oils are considered to be the main constituents in nearly all Peucedanum species and can be responsible for many of their biological activities. (4-5). In this study, volatile oil contents were determined aerial parts and fruits of Peucedanum palimbioides Boiss., P. chryseum (Boiss. &Heldr.) D.F.Chamb., P. graminifolium Boiss., and P. ozhatayiorum Akpulat & Akalın. species which are endemic in Turkey.

MATERIALS AND METHODS:

In this study, essential oils were obtained from aerial parts of the plants (from fruits of P. Chryseum, exceptionally) by hydrodistillation, using Clevenger type apparatus. Essential oil contents of aerial parts and fruits were determined by GC and GC-MS.

RESULTS:

The major contents were α-pinene (71.5%), β-pinene (22.1%), for P. chryseum fruits; α-pinene (66.2%) and β-pinene (25.4%), for P. palimbioides; trans-pinocarveol (7.7%), myrtenol (6.7%), lauric acid (11.9%) and palmitic acid(21.7%) for P. graminifolium; p-cymen-8-ol (6.2%), spathulenol (13.4%), lauric acid (6.4%) and palmitic acid (21.7%) for P. ozhatayiorum species respectively.

CONLUSION:

The composition of the oils present dissimilar variations among the species.

ACKNOWLEDGEMENTS:

This study was supported by Ankara University Scientific Research Council (13L3336009).

REFERENCES:

1. Liang T et al. (2010). Molecules 15(11): 8060-8071.
2. Chamberlain DF (1972). In Davis PH. (ed). Flora of Turkey and the East Aegean Islands In Peucedanum L. Vol.4, pp 478-481, Edinburg, Edinburgh Univ. Press.
3. Altundag E, Ozturk M (2011). Procedia - Social and Behavioral Sciences 19(0):756-777.
4. Sarkhail P (2014). Journal of Ethnopharmacology 156:235-270.
5. Ağalar HG et al. (2015). Natural Volatiles & Essential Oils. 2(4):4-10.

P-108: INFLUENCE OF DIFFERENT EXTRACTION MODE ON THE YIELD OF HYPEROSIDE AND VITEXIN-2-O-RHAMNOSIDE FROM CRATAEGUS MONOGYNA

Ozbilgin, S., Ergene Oz, B., Bahadir Acikara, O., Saltan-Iscan, G.

Ankara University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

Hawthorn (Crataegus spp.) has been used since 1800s for the treatment of heart problems such as hypertension, angina, arrhythmia and congestive heart failure (1, 2). Crataegus spp. contain the flavonoids including hyperoside, vitexin and their glycosides which have been shown to have pharmacological activity (3). The aim of the study is to investigate the influence of the extraction mode on the yield of

bioactive compounds from Crataegus monogyna in order to evaluate plant productivity.

MATERIALS AND METHODS:

Air-dried and powdered aerial parts of C. monogyna were extracted with different ratio of ethanol and methanol in water and with different extraction technics. Vitexin-2-O-rhamnoside and hyperoside were calculated as main compounds in the extracts and the results were compared to each other. The aerial parts of C. monogyna (1 g) were dissolved in 10 mL of methanol and filtered from 0.45 µm filter and directly injected. The stock solution is prepared by dissolving 10 mg vitexin-2-O-rhamnoside and hyperoside in 10 mL methanol (1 mg/mL). The dilutions in five concentrations of the standards (0.1, 0.2, 0.4, 0.5 and 0.7 mg/mL) were diluted from stock solution. The calibration equation was obtained by using five peak areas of standard solutions. Eleven Hawthorn capsules which were coded A1-A11 were purchased from the market in Turkey. The HPLC profiles of the standardized extracts were examined and compared with C. monogyna extract chromatogram.

RESULTS:

It was observed that the amount of extract prepared by maceration with 70% ethanol at 50°C for 30 min was higher. This extract contained 0,2146±0,0002% of the amount of vitexin-2-O-rhamnoside; and the amount of hyperoside was 0.144±0.0232%. In addition, the HPLC profile of the A1, A5 and A7 preparations did not show similarity with the hawthorn extract. Vitexin-2-O-rhamnoside and hyperoside could not be detected in the contents of A1 and A7. In the preparation of A5, a substance which could be a low amount of hyperoside was observed, however, no viteksin-2-O-rhamnoside was detected. In the other preparations, the mentioned substances were not identified.

CONCLUSIONS:

Hyperoside and vitexin-2-O-rhamnoside quantification in different plant extracts was developed and successfully applied to study and optimize extraction protocols. Different extraction methodologies (different temperature, different extraction time, and different extraction mode) were compared under different experimental conditions.

REFERENCES:

1. Brenyo A, Aktas MK (2014). The American Journal of Cardiology, doi: 10.1016/j. amjcard.2013.11.044.
2. Edwards JE, Brown PN, Talent N, Dickinson TA, Shipley PR (2012). Phytochemistry, 79:5-26.
3. Martino E, Collina S, Rossi D, Bazzoni D, Gaggeri R, Bracco F, Azzolina O (2008). Phytochemical Analysis, 19:534-540.

P-109: THE ESSENTIAL OIL COMPOSITION OF THREE ACHILLEA SPECIES USING GS-MS/FID

[1] Akdeniz, M., [2] Senturk, K., [3] Yilmaz, M.A., [3] Temel, H., [1] Bakir, D., [4] Yener, I., [5] Tokolmez, O., [6] Yigitkan, S., [7] Kolak, U., [8] Ertas, A.

[1]The Council of Forensic Medicine, Ministry of Justice, Diyarbakir, Turkey

[2]Dicle University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Diyarbakir, Turkey

[3]Dicle University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Diyarbakir, Turkey

4Dicle University, Faculty of Pharmacy, Department of Analytical Chemistry, Diyarbakir, Turkey

5Mugla Sıtkı Kocman University, Faculty of Science, Department of Chemistry, Mugla, Turkey

6Dicle University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Diyarbakir, Turkey

7Istanbul University, Faculty of Pharmacy, Department of Analytical Chemistry, Istanbul, Turkey

8Dicle University, Faculty of Pharmacy, Department of Pharmacognosy, Diyarbakir, Turkey

INTRODUCTION:

Achillea L. (Asteraceae) is a widely distributed medicinal plant in the world and represented by 140 species in the world (1). Achillea L. species are commonly used in Turkish traditional medicine for the treatment of wounds, bleedings, headache, inflammation, pain, against spasmodic diseases, flatulence, dyspepsia and hemorrhoids for years (1). In this study, it is aimed to determine the essential oil contents of Achillea monocephala, A. nobilis and A. goniocephala species by GC-MS.

MATERIALS AND METHODS:

In this study, the essential oils content of Achillea monocephala, A. nobilis and A. goniocephala were analyzed by GC-MS/FID. The dried aerial parts of species were cut into small pieces and subjected to hydro-distillation with water for 4 h, using a Clevenger-type apparatus to produce essential oils which were dried over anhydrous sodium sulphate and stored at +4°C until required. Identification of the compounds was based on the comparison of their retention times and mass spectra with those obtained from authentic samples and/or the NIST and Wiley spectra as well as the literature data.

RESULTS:

The essential oil contents of A.monocephala, A. nobilis, A. goniocephala species were determined %95.87, %95.31, %96.10, respectively. The major components of A. monocephala were artemisia ketone (31.90%), camphor (12.60%) and β-phellandrene (12.54%). Major components of A. nobilis were eucalyptol (22.89%), chrysanthenone (14.31%) and α-pinene

(8.16%). The major components of A. goniocephala were found to be endo-borneol (30.07%), eucalyptol (25.59%) and camphor (24.45%).

CONCLUSIONS:

It has been determined that there are differences in the major components and diversity of the three species studied in general. But it can be said that the essential oils in the three species studied are rich in monoterpenes.

REFERENCES:

1. Huber-Morath A (1975). In: Davis PH (Ed.), Flora of Turkey and the East Aegean Islands, Edinburgh University Press, Edinburgh, 5:224-252.

P-110: THE ESSENTIAL OIL COMPOSITION OF THYMUS BRACHYCHILUS SUBSP. BRACHYCHILUS AND T. BRACHYCHILUS SUBSP. BAHCESARAYENSIS USING GC-MS/FID

[1] Akdeniz, M., [2] Senturk, K., [3] Firat, M., [4] Yener, I., [4] Varhan Oral, E., [5] Hasimi, N., [4] Seker, Z., [6] Yigitkan, S., [7] Ertas, A.

[1]Dicle University, Faculty of Science, Department of Analytical Chemistry, Diyarbakir, Turkey

[2]Dicle University, Faculty of Pharmacy Department of Pharmaceutical Toxicology, Diyarbakır, Turkey

[3]Yuzuncu Yil University, Faculty of Education, Department of Biology, Van, Turkey

4Dicle University, Faculty of Pharmacy, Department of Analytical Chemistry, Diyarbakir, Turkey

5Batman University, School of Health, Department of Nutrition and Dietetics, 7[2]060, Batman, Turkey

6Dicle University, Faculty of Pharmacy Department of Pharmaceutical Botany, Diyarbakır, Turkey

7Dicle University, Faculty of Pharmacy, Department of Pharmacognosy, Diyarbakir, Turkey

INTRODUCTION:

The genus Thymus L. is a member of Lamiaceae family and represented by 318 species in the world, 40 species in Turkey and 18 of them are endemic for Turkey (45%) (1). In recent years, plant derivatives, especially essential oils, have gained significant interest in academic society and food industry (2). In this study, it was aimed to determine the essential oil contents of Thymus brachychilus subsp. brachychilus and T. brachychilus subsp. bahcesarayensis species by GC-MS.

MATERIALS AND METHODS:

In this study, the essential oils content of T.brachychilus subsp. brachychilus and T. brachychilus subsp. bahcesarayensis were analyzed by GC-MS/FID. The dried aerial parts of species were cut into small pieces and subjected to hydro-distillation with water for 4 h, using a Clevenger-type apparatus to produce essential oils which were dried over anhydrous sodium sulphate and stored at +4°C until required. The essential oils were diluted by dichloromethane (1:3, v/v) before the GC run. Identification of the compounds was based on the comparison of their retention times and mass spectra with those obtained from authentic samples and/or the NIST and Wiley spectra as well as the literature data.

RESULTS:

The essential oil contents of T.brachychilus subsp. brachychilus and T.brachychilus subsp. bahcesarayensis species were determined 95.58%, 98.82% respectively. Major components for T.brachychilus subsp. brachychilus species are eucalyptol (11.05%), geranylacetate (6.1%) and thymol (5.1%), and for T. brachychilus subsp. bahcesarayensis species are linalool (33.92%), thymol (11.02%) and caryophyllene (6.98%).

CONCLUSIONS:

The essential oil contents of the.T.brachychilus subsp. brachychilus and T. brachychilus subsp. bahcesarayensis species were determined. It was seen that T.brachychilus subsp. bahcesarayensis species can be used as a linalool source.

ACKNOWLEDGEMENTS:

The research was funded by grant: DUBAP ECZ.15.003

REFERENCES:

1. Baytop T (1994). Türkiye'de Tıbbi Bitkilerle Tedavi, Nobel Tıp Kitapevleri, Istanbul, Turkey.
2. Ertas et al., (2014). Journal of Agricultural and Food Chemistry 62: 4601–4609.

P-111: THE ANTIBIOFILM ACTIVITY OF ERICA MANIPULIFLORA SALISB.

[1] Omuzbuken, B.,[1] Kacar, A., [2] Avunduk, S.

[1]Dokuz Eylul University, Institute of Marine Sciences and Technology, Izmir, Turkey

[2]Mugla Sitki Kocman University, The Vocational School of Medical Health Services, Mugla, Turkey

INTRODUCTION:

Biofilms can have negative effects on human activities in many ways, including energy waste,heat transfer resistance,requirement for excess equipment capacity, decreased life of equipment, quality control problems, safety problems (1,2). The genus Erica L. (Ericaceae) is represented by more than 700 species in the world, Erica manipuliflora Salisb. are widespread species common in the coastal sides in Turkey (3).

The main objectives of this study were to investigate the antibiofilm activity of the CH2Cl2 extract (EC) obtained from the plant, a major compound: Ursolic

acid (UA) isolated from EC by MIC test against some biofilm bacteria. As far as our literature survey could ascertain,antibiofilm potential of the plant extract,a major secondary metabolite are reported for the first time.

MATERIALS AND METHODS:

A major compound was isolated from EC, elucidated by extensive 1D-and 2D-NMR, mass spectroscopic techniques. Of the fraction EC, a major compound UA were tested against bacteria (Pseudoalteromonas agarivorans,Alteromonas genoviensis, Exiguobacterium homiense, Vibrio lentus) at varying concentrations. Inhibition concentrations of the fractions against marine biofilm bacteria were analyzed with the MIC test (4).

RESULTS:

The phytochemical investigation of EC led to the characterization of one pentacyclic triterpene saponin: Ursolic acid,its' structure was confirmed by literature data (5). As a result of the screening of inhibition concentrations of the extract and compound, the species A. genoviensis (for UA in dilution of 1/1024 corresponded to 2.58 µg/ml;for EC in dilution of 1/1024 corresponded to 3.07 µg/ml),P. agarivorans (same dilution,concentration with A. genoviensis) were determined as the most sensitive bacteria.

CONCLUSIONS:

It was also determined that it would be worth doing further studies in which pure substances to be obtained could be used as an antifouling additive in industrial areas to prevent marine biofilms.

REFERENCES:

1. Characklis WG (1990). Microbial biofouling control. In: Characklis WG and Marshall KC., Biofilms.New York:Wiley & Sons, pp 585–633.
2. Tang RJ, Cooney JJJ (1998).Industrial Microbiology and Biotechnology. 20, 275–280.
3. Stevens,PF (1978). In: Davis, P.H. (Ed.), Erica L. in Flora of Turkey and the Aegean Islands, vol. 6. University Press, Edinburgh, pp. 95–97.
4. Zgoda JR, PorterJR (2001). Pharmaceutical Biology 39(3):221–225.
5. Ayuso Gonzalez MJ, Reyes Ruiz M, Toro Sainz MV (1991). Anales de la Real Academia de Farmacia, 57: 419–423.

P-112: THE ANTIFUNGAL ACTIVITY OF ERICA MANIPULIFLORA SALISB.

[1] Avunduk, S., [2] Omuzbuken, B., [2] Kacar, A.

[1]Mugla Sitki Kocman University, The Vocational School of Medical Health Services, Mugla, Turkey

[2]Dokuz Eylul University, Institute of Marine Sciences and Technology, Izmir, Turkey

INTRODUCTION:

Fungal infections have emerged as a growing threat to human health.Two important reasons for this are the increasing number of HIV infected patients and the number of patients being treated with cancer chemotherapy drugs (1). The genus Erica L.(Ericaceae) is represented by more than 700 species in the world, mainly found in the South Africa, furthermore Mediterranean and West European (2). Our present work was designed to assess the in vitro antifungal activity of Erica manipuliflora Salisb. extract (EC), the n-BuOH fractions (EBA-EBE) and a major secondary metabolite:Ursolic acid on Candida albicans.

MATERIALS AND METHODS:

All the extracts (n-Hexane,CH2Cl2,MeOH) were prepared from the powdered dried aerial parts of the plant by extracting with Soxhlet apparatus.The MeOH extract was partitioned with n-BuOH. The five fractions codded EBA-EBE were obtained from the n-BuOH extract. A major compound was isolated from the CH2Cl2 extract(EC), elucidated by extensive 1D-,2D-NMR, mass spectroscopic techniques. Of the fractions,EBA-EBB-EBC (flavonoids, phenylethanoid glycosides), EBD-EBE (triterpenoid saponins),EC,Ursolic acid were tested against C. albicans at varying concentrations.Inhibition concentrations of the fractions were analyzed with disk diffusion method (3).

RESULTS:

In this study, we have isolated a pentacyclic triterpene saponin (Ursolic acid) from the CH2Cl2 extract,its' structure was confirmed by literature data (4). As a result of the screening of inhibition concentrations of the samples,Ursolic acid(in dilution 1/16 corresponded to 0.16 mg/ml),EC extract(in dilution 1/4 corresponded to 0.78 mg/ml) and the fraction EBA (in dilution 1/16 corresponded to 0.47 mg/ml) were determined as the most effective samples against Candida albicans.

CONCLUSIONS:

C.albicans is known to have resistance mechanisms against antimicrobial drugs.The detection of the interactions with relatively under-researched biomolecules are important to overcome the problem of these resistance mechanisms.Therefore, studies on biomolecules need constantly progress to reduce for resistance of C.albicans to antimicrobial drugs.

Our data extended the basic for the designing and modeling of new compounds as antimicrobial agents.

REFERENCES:

1. Georgopapadakou NH, Walsh TJ (1996). Antimicrobial Agents and Chemotheraphy,40:279-91.
2. Stevens,PF (1978). In:Davis, P.H. (Ed.), Erica L. in Flora of Turkey and the Aegean Islands, vol. 6. University Press,Edinburgh,pp.95–97.
3. NCCLS(National Committee for Clinical Laboratory Standards)(1999).Performance standards for antimicrobial susceptibility testing. In Ninth Informational Supplement Pennsylvania USA:M 100-S9.
4. Ayuso Gonzalez,MJ, Reyes Ruiz,M, Toro Sainz,MV(1991).Anales de la Real Academia de Farmacia,57,419–423.

P-113: FATTY ACID COMPOSITION OF BLACK CUMIN (NIGELLA SATIVA L.) SEED OIL PRODUCTS FROM TURKEY

[1] Aslan Erdem, S., [2] Isik, S., [3] Kartal, M.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

[2]Near East University, Faculty of Pharmacy Department of Analytical Chemistry, Nicosia, TRNC

[3]Bezmi Alem Vakıf University, Faculty of Pharmacy, Department of Pharmacognosy, Istanbul, Turkey

INTRODUCTION:

Black cumin seeds and the oil extracted from the seeds are generally safe for use as a home remedy to prevent diseases and promote good health. According to recent researches, black cumin seed oil's major fatty acids are linoleic, oleic and palmitoleic acids (1-4). In this study we aimed to examine the compositions of some of the black cumin oil brands that are sold in Turkish market.

MATERIALS AND METHODS:

Seed oils were supplied from local markets in Ankara. Fatty acid methyl esterification (FAME) was conducted by using BF3/MeOH reagent. Chromatographic analysis was carried out on Agilent 6890N Network GC system combined with Agilent 5973 Network MS Detector (GC-MS). The capillary column used was HP Innowax Capillary;60.0m ×0.25mm×0.25µm. Run time for the analysis was 35min (5).

RESULTS:

Fatty acid profile was given in Table 1. Major fatty acids (linoleic, oleic and palmitic acids) were observed in all samples. Even though Samples 6 and 10 tried to be esterified three times, a chromatogram could not be obtained.

Table 1. Fatty acid profiles of black cumin fixed oils

Fatty Acids	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6	Sample 7	Sample 8	Sample 9	Sample 10
C14:0	-	-	-	-	0.153	-	-	0.144	0.160	-
C16:0	10.556	8.068	7.292	8.185	12.413	-	12.888	12.129	12.626	-
C16:1	-	-	-	-	0.168	-	-	0.172	0.174	-
C18:0	3.022	0.892	3.273	3.644	3.075	-	2.977	3.40	3.346	-
C18:1	33.080	51.831	41.066	28.947	25.310	-	25.982	25.315	25.067	-
C18:2	52.120	35.276	48.368	56.979	55.734	-	58.154	55.478	55.614	-
C18:3	0.569	3.934	-	0.567	0.206	-	-	0.342	0.218	-
C20:0	-	-	-	0.210	0.254	-	-	0.216	-	-
C20:2	0.654	-	-	0.751	2.687	-	-	2.804	2.795	-
C22:2	-	-	-	0.717	-	-	-	-	-	-

CONCLUSIONS:

Analyzed samples are found to be rich in especially oleic and linolenic acids. GC-MS analysis of the fatty acids obtained from ten commercial seed oil showed that the qualitative composition of the fatty acid profile was almost identical with each other.

REFERENCES:

1. Ashraf M, Qasim, A., Zafar, I. (2006) J.Sci Food Agric. doi:10.1002/jsfa.2426.
2. Nickavar B, Mojab F, Javidnia K, Amol MAR (2003). Zeitschrift fur Naturforsch-Sect CJ Biosci.
3. Cheikh-Rouhou S, Besbes S, Hentati B, Blecker C, Deroanne C, Attia H (2007). Food Chem., 101(2):673-681.
4. Tulukcu E (2011). African J Agric Res. 6(4): 892-895.
5. Ugur A, Suntar I, Aslan S, Orhan IE, Kartal M, Sekeroglu N, Esiyok D, Sener B (2010). Pharmacogn Mag., 6(24): 305.

P-114: ENZYME INHIBITORY, ANTIOXIDANT ACTIVITES AND PHYTOCHEMICAL STUDIES ON JUNIPERUS MACROCARPA

Orhan, N., Pekacar S., Ozupek, B., Deliorman Orhan, D.

Gazi University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

Juniperus macrocarpa Sibt. & Sm. (Cupressaceae) is one of the Juniper species growing in Turkey that is used for medicinal purposes. We aimed to evaluate in-vitro antidiabetic and antioxidant activities of the extracts prepared from leaves and branches of J. macrocarpa.

MATERIALS AND METHODS:

The leaves and branches of J. macrocarpa, were collected from İzmir on June 2010. α-amylase and α-glucosidase inhibitory effects and antioxidant activities of the water, ethyl acetate, and methanol extracts of the plant were evaluated. Antioxidant activities of the extracts were determined by DPPH radical scavenging, ferric reducing, metal chelating and phosphomolybdenum assays. Additionally, total phenol and flavonoid contents of the extracts were investigated (1).

RESULTS:

All extracts showed excellent and dose dependent inhibitory effect on α-glucosidase enzyme. Moreover, branch (99.78 ± 0.03 %) and leaf methanol extracts (99.16 ± 0.45%) were more effective than Acarbose (98.88 ± 0.07%) at 1 mg/ml. Additionally, the extracts rich in flavonoids (9.99-45.16 mg quercetin equivalent/g extract) and phenolics (92.18-230.54 mg gallic acid equivalent/g extract) showed remarkable antioxidant activity.

CONCLUSIONS:

It has been determined that J. macrocarpa leaves and branches are natural source of antidiabetic and antioxidant activity, which can be a subject of in-vivo research.

REFERENCES:

1. Orhan N, Gokbulut A, Deliorman Orhan D, (2017). South African Journal of Botany, 111:86-92.

P-115: ANTIOXIDANT CAPACITY AND TOTAL PHENOLIC CONTENT OF LAVANDULA STOECHAS L. SUBSP. STOECHAS

Coban S, Yuzbasioglu M, Kuruuzum-Uz A.

Hacettepe University, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

Lavandula stoechas L. subsp. stoechas (LS) belongs to the Lamiaceae family and occurs naturally in Mediterranean countries. The major secondary metabolites of LS are terpenoids and phenolic constituents. Essential oil of lavender has been used in folk medicine since ancient times and relaxing, sedative, antistress, anticonvulsive, spasmolytic, anticancer, repellent, antibacterial, antimicrobial and antifungal properties are known, also is used for cosmetic purposes due to its scent and aroma. The studies on lavender has focused on essential oils. In this study, we aimed to determine the antioxidant capacity and total phenolic content of LS hydrophilic extracts.

MATERIALS AND METHODS:

The aqueous and aqueous-ethanolic (70%) extracts were prepared from the aerial parts of LS collected from Muğla-Fethiye in 2017. The extracts of LS were investigated for their antioxidant capacities using nitric oxide radical (NO), superoxide radical (SO), 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical, 2,2'-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radical scavenging activities and Ferric Reducing Antioxidant Power (FRAP), Cupric Ion Reducing Antioxidant Capacity (CUPRAC) assays. The total phenolic contents were measured by Folin–Ciocalteau assay.

RESULTS:

The IC50 values for DPPH, SO, NO radical scavenging activities were measured as 43.01mg/mL, 43.02mg/mL, 317.13mg/mL for aqueous extract and 50.19 mg/mL, 48.35mg/mL, 243.05mg/mL for aqueous-ethanolic extract, respectively.CUPRAC, FRAP and ABTS antioxidant capacities were determined as118.258 mg gallic acid/g, 783.33 mg trolox/g, 277 mg trolox/g for aqueous extract and 172.8548 mg gallic acid/g, 926.44 mg trolox/g, 354.4 mg trolox/g for aqueous-ethanolic extract, respectively.The total phenolic contents were found as 152.2 mg gallic acid/g for aqueous extract and 180.1 mg gallic acid/g for aqueous-ethanolic extract.

CONCLUSIONS:

The extracts of LS are similar when evaluated in terms of antioxidant capacity and total phenolic content of aqueous-ethanolic extract was found more.

REFERENCES:

1. Lis Balchin M (2002). Lavander. The Genus Lavandula. Medicinal and Aromatic Plants–Industrial
2. Profiles, Taylor & Francis, Great Britain, pp 17-124.
3. Zhang Q, Zhang J, Shen J et al., (2006). Journal of Applied Phycology, 18:445–450.
4. Genc Y, Yuzbasioglu M, Harput US, Kuruuzum Uz A (2012). FABAD Journal of Pharmaceutical Sciences, 37: 17-22.
5. Buyuktuncel E (2013). Marmara Pharmaceutical Journal.17(2):93-103.
6. Apak R, Guclu K, Ozyurek M et al., (2006). International Journal of Food Sciences and Nutrition, 57:292-304.
7. Ozgen U, Mavi A, Terzi Z, Yildirim A, Çoskun M, Houghton PJ (2006). Pharmaceutical Biology, 44:107-112.

P-116: CYTOTOXIC ACTIVITY OF ETHANOLIC EXTRACT AND SOME FRACTIONS OF THE ROOTS OF FERULAGO MACROSCIADIA BOISS & BALANSA AGAINST SW480 AND MCF-7 CANCER CELL LINES

[1] Gunbatan, T., [2] Bakar, F., [1] Gurbuz, I., [3] Kilic, C.S., [1] Karakucuk, M., [4] Duman, H.

[1]Gazi University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey

[3]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

4Gazi University, Faculty of Science, Department of Biology, Ankara, Turkey

INTRODUCTION:

Cancer has become the reason for high morbidity and mortality rates throughout the world (1). Therefore scientists are searching for efficient treatment alternatives, including medicinal plants. As a result of recent studies on herbal resources, some Ferulago species, i.e. F. angulata (Schlecht) Boiss. was revealed to possess anticancer activity against lymphoma and leukemia cells (2). Therefore we decided to study the cytotoxic activity of F. macrosciadia, an endemic species for our country, against different cancer cell lines.

MATERIALS AND METHODS:

In this study, ethanolic extracts of the roots of F. macrosciadia Boiss & Balansa, an endemic species for Turkey (3) and its buthanol, dimethyl chloride, ethylacetate fractions and aqueous remainder were tested for their cytotoxic activities against SW480 (colorectal carcinoma) and MCF-7 (breast carcinoma) cell lines in concentrations of 1, 0.1, 0.05, 0.025, 0.01 mg/ml via (3-(4,5-dimethylthiazolyl-2)-2, 5-diphenyltetrazolium bromide (MTT) assay. Cell viabilities were measured with spectrophotometry (at 540 nm) and the nontreated cells in the control group were used as reference.

RESULTS:

Dimethyl chloride fraction was found to be more active compared to others and the total extract; The viable cell amount was has significantly decreased (15.06±1.64% and 45.15±6.50%, $p<0.05$) at 0.1 mg/ml treated concentration in SW480 and MCF-7 cells, respectively.

Conclusion: According to our results, we can conclude that F. macrosciadia is cytotoxic against the above mentioned cell lines and further studies have to be performed to isolate and identify the responsible active substances.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG 115S364).

REFERENCES:

1. Jemal A, Tiwari RC, Murray T, Ghafoor A, Samuels S, Ward E, Feuer EJ, Thun MJ (2004). CA Cancer J Clin, 54: 8-29.
2. Shahneh FZ, Baradan B, Orangi M, Zamani F (2013). 3(2): 453-455.
3. Pesmen H (1972). In: Davis PH. (ed.) Flora of Turkey and the East Aegean Islands, University Press, Edinburgh, Vol 4, pp 462-464.

P-117: COMPARATIVE LC-MS/MS STUDIES ON THREE DIFFERENT DIGITALIS SPECIES

[1] Kutluay, V.M., [2] Goger, F., [2] Kirimer, N.,[1] Saracoglu, I.

[1]Hacettepe University, Department of Pharmacognosy, Ankara, Turkey

[2]Anadolu University, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

In the Flora of Turkey, the genus Digitalis is represented by nine species (1). In this research D. davisiana Heywood, D. grandiflora Miller and D. viridiflora Lindley were compared phytochemically via LC-MS/MS analysis. Phytochemical studies on Digitalis genus have already identified cardioactive glycosides, flavonoids, anthroquinones, phenylethanoid glycosides and other similar phenolic compounds (2).

MATERIALS AND METHODS:

Plants were collected and voucher specimens for all plants were deposited in Hacettepe University Faculty of Pharmacy Herbarium with codes HUEF11004, HUEF13007, HUEF13008. Aerial parts of the selected plants were extracted by methanol. Methanolic extracts and 18 standard compounds applied to a new LC-MS/MS assay developed for this research. LC-MS/MS system: HPLC (Shimadzu 20A), column [Intersil ODS column (4.6 x 250 mm, 5 µm particle size), UV detector (SPD20A Shimadzu DAD Detector) and 3200 Q TRAP (AB Sciex, Toronto, Canada) with electron spray ionization interface (ESI). The mobile phase was acetonitrile:water:formic acid (10:89:1, v/v/v) (solvent A) and acetonitrile:water:formic acid (89:10:1, v/v/v) (solvent B) at a flow rate of 0.5 mL/min. The gradient elution started with 10% solvent B at 0 min, 100% solvent B reached at 40 min. The column temperature was kept at 40ºC.

RESULTS:

D.davisiana, D. grandiflora and D.viridiflora were compared for their secondary metabolites through 24 compounds. Lugrandoside, isolugrandoside,

maxoside, digidavisoside B, isoacteoside, chyrsoeriol, apigenin, luteolin, luteolin glucuronide, apigenin glucuronide, luteolin-7-O-glucoside were detected in all extracts. Lugrandoside and maxoside were detected as major compounds. When the results were evaluated, from total 24 compounds 19, 17 and 14 compounds were detected in D. davisiana, D. grandiflora and D. viridiflora respectively.

CONCLUSIONS:

These results showed us that even though all extracts were similar in content, D. davisiana was found to be more rich in secondary metabolite content. Our findings support chemotaxonomic and phylogenetic studies on Digitalis genus and Plantaginaceae family.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK 2211/A program.

REFERENCES:

1. Davis PH, (1978). Flora of Turkey and the East Aegean Islands (Volume 6). Edinburgh University Press, Edinburgh.
2. Taskova RM et al., (2005). Phytochemistry, 66: 1440-1447.

P-118: LIVER X RECEPTOR AGONIST ACTIVITY OF SOME MEDICINAL PLANTS FROM TURKEY

[1] Kutluay, V.M., , [1] Genc, Y., [1] Dogan, Z., [2] Inoue, M., [1] Saracoglu, I.

[1]Hacettepe University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

[2]Aichi Gakuin University, Faculty of Pharmacy, Laboratory of Medicinal Resources, Nagoya, Japan

INTRODUCTION:

Nuclear receptors are regulators of gene transcription and intracellular function. They control various biological events. Liver X receptors (LXR) play role in de novo synthesis of cholesterol, excretion and detoxification of bile acids, or lipids, glucose homeostasis and neurological functions. LXR is also known to play an inhibitory role in inflammatory signaling pathway (1). Turkish medicinal plant species, Plantago holosteum, P. major, P. lagopus, P. scabra and Scutellaria salviifolia were investigated for their LXRα agonist activity.

MATERIALS AND METHODS:

5 plant extracts were screened for liver X receptor (LXR) agonist activity using LXRE reporter gene assay (2). HEK293 cells were used in LXRE reporter gene assay. Plants were collected and voucher specimens for all plants were deposited in Hacettepe University Faculty of Pharmacy Herbarium. Air-dried aerial parts of the plants were extracted with methanol. Methanol was evaporated under vacuum to yield extract. Then it was dissolved in water and partitioned with petroleum ether to remove chlorophylls and other lipophilic compounds. The aqueous fractions were lyophilized and used in the biological activity tests at a concentration of 100 µg/ml.

RESULTS:

In this study, LXRα agonist, T09011317 was used as positive control at the concentrations of 1, 10 and 100nM. The results were given as fold induction values normalized by β-galactosidase. P. holosteum, P. major, P. lagopus, P. scabra extracts showed weak LXRα agonist activity with the fold values in a range of 0.95-1.39. P. major showed highest agonist activity between Plantago species. Scutellaria salviifolia extract has a fold value of 2.37.

CONCLUSIONS:

In this study, the potential LXRα agonist activity of extracts were evaluated. The agonist activity of Scutellaria salviifolia was found to be comparable with the positive control T09011317. While the agonist activity of tested Plantago species found to be lower. Scutellaria species are widely used as traditional medicine especially in eastern Asia due to its anti-inflammatory effects. As LXRα plays important role in inflammation, anti-inflammatory effect of Scutellaria species may be due to this pathway.

ACKNOWLEDGEMENTS:

Vahap Murat Kutluay was supported by a grant of TUBITAK 2214/A program.

REFERENCES:

1. Viennois E et al., (2012). Molecular and Cellular Endocrinology, 351: 129-141.
2. Nakashima K et al., (2014). Biochimica et Biophysica Acta, 1840: 3034-3041

P-119: COMPARATIVE LC-MS/MS STUDIES ON PHYTOCHEMICAL CONTENTS OF THREE ENDEMIC SCUTELLARIA SPECIES.

[1] Dogan, Z., [2] Goger, F., [2] Kirimer, N.,[1] Saracoglu, I.

[1] Hacettepe University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

[2] Anadolu University, Faculty of Pharmacy, Department of. Pharmacognosy, Ankara, Turkey

INTRODUCTION:

Scutellaria is represented by 32 taxa and 14 of them are endemic in the flora of Turkey (1). In the revision of the genus, there are three sections; sect. Scutellaria, Salviifoliae, Lupulinaria. Scutellaria species are one of the most popular herbs in traditional Chinese medicines and are used in the treatment of gastrointestinal disorders, inflammation, cardiovascular diseases, bacterial and viral infections (2). In the present study, three endemic Scutellaria species (S. salviifolia Benth., S. glaphyrostachys

Rech.f. and S. rubicunda Stapf. subsp. brevibracteata) selected from two different section (sect. Scutellaria and sect. Salvifoliae) were studied by LC-MS/MS to evaluate differences in phytochemical compositions of sections.

MATERIALS AND METHODS:

Plants are collected and voucher species are deposited in Hacettepe University Faculty of Pharmacy Herbarium with codes HUEF 12003, 14066, 14065. LC-MS/MS analyses were performed on the aqueous fractions of methanol extracts of the titled plants. LC-MS/MS system: HPLC (Shimadzu 20A), column [Intersil ODS column (4.6 x 250 mm, 5 µm particle size), UV detector (SPD20A Shimadzu DAD Detector) and 3200 Q TRAP (AB Sciex, Toronto, Canada) with electron spray ionization interface (ESI). The mobile phase was acetonitrile:water:formic acid (10:89:1, v/v/v) (solvent A) and acetonitrile:water:formic acid (89:10:1, v/v/v) (solvent B) at a flow rate of 0.5 mL/min. The gradient elution started with 10% solvent B at 0 min, 100% solvent B reached at 40 min. The column temperature was kept at 40ºC.

RESULTS:

When chromatograms of aqueous extracts were compared; phytochemical profiles of S. glaphyrostachys and S. rubicunda subsp. brevibracteata, which belong to sect. Scutellaria, were seemed to be quite similar to each other. While the chemical content of the S. salviifolia (from sect. Salviifoliae) was different from the other two extracts. Isolation and LC-MS/MS studies were evaluated together and it was found that the Salviifoliae section was rich in phenolic compounds, while the Scutellaria section contains iridoid glucosides more than phenolic compounds. Luteolin, luteolin-7-O-β-glucuronide and baicalin were found as common compounds in all tested aqueous extracts.

CONCLUSIONS:

This study supports to botanical revision of Scutellaria genus grown in Turkey by phytochemically, too. Clarification of chemical compositions of three Scutellaria species in detailed contributed to the chemotaxonomy of the genus.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (2211-C) and HUBAB (TDK-2017-14236)

REFERENCES:

1. Cicek M. (2008) Turkiye *Scutellaria* L. (Lamiaceae) Cinsinin Revizyonu [Doktora Tezi]. Ankara: Ankara Universitesi.
2. Shang et al., (2007). J Ethnopharmacol. 128(2):279-313.

P-120: IN VITRO ALPHA-GLUCOSIDASE INHIBITORY ACTIVITY OF QUERCUS MACRANTHERA SUBSP. SYSPIRENSIS

[1] Gozcu, S., [2] Yuca, H., [2] Dursunoglu, B., [2] Guvenalp, Z.

[1] Erzincan University, Faculty of Pharmacy, Department of Pharmacognosy, Erzincan, Turkey

[2] Atatürk University, Faculty of Pharmacy, Department of Pharmacognosy, Erzurum, Turkey

INTRODUCTION:

There are 24 species and 15 subspecies of the genus Quercus in flora of Turkey. Quercus macranthera subsp. syspirensis (Fagaceae) is an ecologically important endemic species and known as İspir oak (1). It has been reported that it contains some phenolic compounds such as tannins (epicatechin, catechin) in its shell (2), and shows antioxidant and antimicrobial activities (3,4). In this study, determination of the α-glucosidase inhibitory activity of Quercus macranthera subsp. syspirensis fruits is aimed.

MATERIALS AND METHODS:

In the present study, the methanol extract of Quercus macranthera subsp. syspirensis fruits and its fractions prepared by n-hexane, chloroform, ethyl acetate, n-butanol and water respectively, were investigated for their α-glucosidase inhibitory activities using the method of Tao et al., (5).

RESULTS:

The ethyl acetate fraction showed the best α-glucosidase inhibitory activity with 89.716 % (IC50= 0.0052 mg/ml) value when compared with the standard compound acarbose that displayed 0.45 % inhibitory activity (IC50= 3.3642 mg/ml) at 25 µg/ml concentration. n-Butanol, methanol, chloroform, n-hexane extracts showed 88.577% (IC50 = 0.0065 mg/ml), 86.703 % (IC50 = 0.0200 mg/ml), 40.659 % (IC50 = 0.0918 mg/ml), 36.585 % (IC50 = 0.1159 mg/ml) inhibitory activity at the same concentration, respectively. However, the water extract showed no inhibition on α-glucosidase.

CONCLUSIONS:

These results indicate that the ethyl acetate extract has a high potential for α-glucosidase inhibitory activity.

ACKNOWLEDGEMENTS:

This study was supported by The Foundation of Ataturk University (2016/121).

REFERENCES:

1. Güner et al., (2012). In: Turkiye Bitkileri Listesi (Damarlı Bitkiler), Nezahat Gokyigic Botanik Bahçesi Yayınevi. İstanbul, pp 506-511.
2. McCue et al., (2005). Journal of Food Biochemistry, 29:278-294.

3. Marles RJ, Farnsworth NR (1995). Phytomedicine, 2:37.
4. Aguilara et al., (1998). Journal of Ethnopharmacology, 61:101-110.
5. Tao et al., (2013). Biomedical Chromatography, 27:48-155.

P-121: DIFFERENCES BETWEEN GG4 MOTIFS ON TRPM2 ION CHANNELS OF HUMAN, RAT AND MOUSE.

[1] Cakmak, A., [2] Aydin, S.

[1] Bozok University, Faculty of Medicine, Department of Pharmacology, Yozgat, Turkey

[2] Anadolu University, Faculty of Pharmacy, Department of.Pharmacology, Eskisehir, Turkey

INTRODUCTION:

Pain is an important physiopathological signal, originating from pain signal generating receptors and ion channels. Transient Receptor Potential (TRP) channels are ligand-gated ion channels which are shown to play role in various functions including inflammation and pain (1). TRPM2 is a member of TRPM family involved in pain and described as a chanzyme but its mechanism is not well known (2). The presence and important of GXXXG (GG4) motifs are shown on many proteins (3). The aim of this study was to investigate the presence and location of GG4 motifs on TRPM2 ion channels.

MATERIALS AND METHODS:

The protein sequences (TRPM2_HUMAN, TRPM2_MOUSE and TRPM2_RAT) were downloaded from uniprot database (www.uniprot.org). Ion channel sequences were extracted using Slackware GNU/Linux operating system. R/Bioconductor packages, Protr. Bio3d and ClustalW were used for alignment of proteins, statistical evaluation and plotting. Swiss-model, Swiss Pdb-viewer were used for 3D modelling.

RESULTS:

The results of our investigations showed the presence of GG4 motifs on the human, mouse and rat TRPM2 ion channels. Alignment of the ion channels showed %82 similarity. Difference for number and locations of GG4 motifs were found using GNU/Linux bash commands. There were 2 GG4 motifs on human and mouse TRPM2, whereas 3 GG4 motifs were found on rat TRPM2 ion channel. Of these GG4 motifs, only one of them (GSHTG) was found on all of the species (human, mouse and rat) and at the same location of the proteins.

CONCLUSIONS:

The number of GG4 motif for the human and mouse TRPM2 ion channels was similar, but differed from the rat TRPM2 ion channel. Since role of the motif on ligand-TRP channels is very difficult by wet lab experiments (3), the in silico results of our investigation suggest more reliable results will be obtained using mice but not rats in pain research where TRPM2 ion channels are involved.

REFERENCES:

1. Dai Y (2016). Semin Immunopathol, 38:277-291.
2. Tan CH, McNaughton PA(2018). Pflugers Arch, https://doi.org/10.1007/s00424-018-2139-7
3. Mueller BK, Subramaniam S, Senes A (2014). Proc Natl Acad Sci U S A. 111, E888-E895.

P-122: THE NORMALIZATION OF CONTRACTILE RESPONSE IN DIABETIC RAT AORTA

[1] Muderrisoglu, AE., [1] Erdogan, BR., [1] Karaomerlioglu, I., [2] Martin, MC., [1] Arioglu Inan, E.

[1] Ankara University, Department of Pharmacology, Ankara, Turkey

[2] Johannes Gutenberg University, Department of Pharmacology, Mainz, Germany

INTRODUCTION:

Vascular dysfunction is an important feature of diabetes. Thus, the accurate evaluation of vascular function is crucial. In vitro organ bath experiments have been usually used to determine contractile response in the thoracic aorta. However, the length and the weight of the aorta does not seem to be unique in each experiment. Therefore, it is essential to normalize the contractile response. Various normalization parameters such as cross-sectional area (CSA) (1,2), weight or length of the rings have been used so far to exclude these differences. The aim of our study was to compare different approaches to determine the most appropriate normalization parameter for the contractile response of the aorta.

MATERIALS AND METHODS:

6-week old male 21 Sprague Dawley rats were used in this study. Some of them (n=17) were fed with high fat diet. After 4 weeks, the rats fed with high fat diet were injected with STZ (35 mg/kg, ip) to induce experimental type 2 diabetes model. 2 weeks after STZ injection, some of the diabetic rats were treated with Dapagliflozine (1mg/kg, orally). After 8 week-treatment period, all rats were euthanasied. The thoracic aorta was dissected and the connective and adipose tissues were removed. A precontraction was induced with 80 mM KCl and the cumulative concentration-response curve of phenylephrine (10 nM - 30 uM) was generated. At the end of the each experiment, the weight and the length of the rings were measured and the CSA was calculated as described previously (2). CSA was used to normalize aortic wall thickness differences and aneurysms.

RESULTS:

r2 values for each normalization parameters

	CSA	Weight	Length
Plateau KCl	0,04541	0,01691	0,01158
Plateau phenylephrine	0,0001977	0,02464	0,06948
Emax phenylephrine	0,03242	0,008063	0,005849

CONCLUSIONS:

All of the three normalization approaches seem to have poor correlation with contraction responses. Thus, we conclude that increasing sample size of experiments could help to further explain this discrepancy.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Ankara University (BAP16L0237006)

REFERENCES:

1. 1.Kristek F, Cacanyiova S, Gerova M (2009). Journal of Physiology and Pharmacology, 60 (2): 21-27.
2. Pieper GM, Langenstroer P, Siebeneich W (1997). Cardiovascular Research, 34: 145-156.

P-123: EFFECTS OF ALISKIREN TREATMENT ON CARDIAC MYOCYTE DYSFUNCTION IN A RAT MODEL OF INSULIN RESISTANCE

[1] Tufan, C., [1] Tarhan, N., [1] Ozansoy, G., [2] Ceylan Isik, A., [1] Kayki Mutlu, G.,[1] Ari, N.

[1] Ankara University, Faculty of Pharmacy, Department of Pharmacology, Ankara, Turkey

[2] Yıldırım Beyazıt University, Department of.Medical Pharmacology, Ankara, Turkey

INTRODUCTION:

Cardiovascular complications are the most common complications of insulin resistance (IR). The use of renin-angiotensin-aldosteron system (RAAS) blockers in patients with IR or diabetes and hypertension has positive effects and is recommended by guidelines. Aliskiren (ALI) is the only available direct renin inhibitor in the market approved for the treatment of hypertension (1). However, the efficacy of ALI in IR-induced cardiomyocyte dysfunction remains to be defined. The aim of this study is to investigate whether ALI tretment has positive effects on IR-induced cardiomyocyte dysfunction.

MATERIALS AND METHODS:

IR was induced in male Wistar rats by high-fat diet (HFD) feeding for 20 weeks. Oral administration of ALI (50 mg/kg, daily) or vehicle was started in the last 12 weeks. At the end of treatment period oral glucose tolerance test (OGTT) was carried out. Blood pressure, heart rate were measured by non-invasive method. Ventricular cardiomyocytes were isolated and contractile properties including cell peak shortening (PS), time to PS (TPS), time to 90% relengthening (TR90) and maximal velocity of shortening/relengthening (± dL/dt) were analysed using video-based edge detection (2).

RESULTS:

Cardiomyocytes from HFD group displayed significantly reduced ± dL/dt associated with prolonged duration of TPS and TR90. ALI treatment had overall positive effects on cardiomyocyte dysfunction. Furthermore ALI treatment significantly improved the metabolic parameters (blood glucose and serum insulin levels, OGTT), systolic blood pressure, heart rate, and body weight gain in HFD group.

CONCLUSIONS:

Our data suggest that renin inhibition by ALI has protective effect on cardiomyocyte dysfunction in IR model of rat through a decrease in IR. We need comparative benefit studies with ALI and the drugs which inhibit the RAAS cascade by different mechanisms.

ACKNOWLEDGEMENTS:

This study was supported by Ankara University (12B3336006)

REFERENCES:

1. Pantzaris ND, Karanikolas E et al., (2017). Journal of Clinical Medicine, 61:2-19.
2. Ren J, Zhu BH et al., (2008). Obesity, 16:2417-23.

P-124: CLINICAL PHARMACIST'S CONTRIBUTION TO ROUTINE TREATMENT IN INTENSIVE CARE UNIT

[1] Uysal, C., [1] Savas, M., [1] Balli, N., [1] Celiker, A., [1] Demirkan, K., [2] Topeli Iskit, A.

[1]Hacettepe University, Faculty of Pharmacy, Department of Clinical Pharmacy, Ankara

[2]Hacettepe University, Faculty of Medicine, Department of Internal Medicine, Intensive Care Unit, Ankara

INTRODUCTION:

The contribution of the clinical pharmacist to the intensive care unit (ICU) has been accepted in many countries since 1960s. This contribution has often been related to prescribing errors, adverse drug effects, cost, length of hospital stay, and mortality. The

purpose of this study is to evaluate the contribution of the clinical pharmacist to routine treatment in ICU in Turkey as pioneering this sentence seems to be incomplete (1,2).

MATERIALS AND METHODS:

This prospective cross-sectional study was conducted by clinical pharmacy students from October 1, 2017 to April 1, 2018 at the 9-bed tertiary hospital ICU. All patients over the age of 18 years were included in the study. The clinical pharmacist interventions during patient visits with the physicians and interventions' acceptance rate were evaluated and classified according to the Pharmaceutical Care Network Europe - Classification V 8.01.

RESULTS:

Thirtyeight of the 72 patients in ICUs were followed and 31 recommendations were made for these 38 patients. The number of suggestions per patient was found as 0.82. While 67.7% of the proposals were accepted and implemented, 16.1% were accepted but not implemented or partially implemented. The problems identified in the interventions reached a solution rate of 74.2%. Most of the recommendations (77.4%) were found to be related to dose error. In addition, interventions have been made regarding drug selection, drug form and therapeutic drug monitoring.

CONCLUSION:

Clinical pharmacist's contribution in the ICU multidisciplinary team would be beneficial to improve the management of drug related problems.

REFERENCES

1. Higby G (1997). Pharmacy in the American century. Pharmacy Times, 63:16–24
2. Chant C, Dewhurst NF, et al., (2015). Do we need a pharmacist in the ICU? Intensive Care Med; 41:1314-1320.

P-125: THE FORMATION OF COMPLEXES BETWEEN GLUTATHIONE REDUCED-OXIDIZED AND COPPER IONS

Catapano, MC., Mladěnka, P.

Charles University, Faculty of Pharmacy, Department of Pharmacology and Toxicology, Hradec Králové, Czech Republic

INTRODUCTION

Glutathione (GSH) is a tripeptide of glutamate, cysteine and glycine (1). GSH as a low molecular mass antioxidant is the most abundant intracellular thiol which plays an essential role in maintaining the intracellular redox environment. Glutathione exists in both reduced (GSH) and oxidized (GSSG) states. Under oxidative stress conditions, GSH is generally oxidized to GSSG. It is less known that GSH is also a copper chelator (2). The aim of this study was to analyze the interaction of glutathione in both reduced and oxidized states with copper ions (Cu^{2+} and Cu^{+}).

MATERIALS AND METHODS:

First, absorption spectra were scanned, and the wavelength of the absorption maximum of pure GSH/GSSG and their Cun+ complexes were determined. The assessment of the interaction with copper was performed at four (patho)physiologically relevant pH values (4.5. 5.5, 6.8 and 7.5) in both competetive (hematoxylin and bathocuproine) and non-competetive (Job's method (3) and Complementary approach (4)) settings in order to find the most probably stoichiometry.

RESULTS:

Under most conditions in which the metal complex was formed, the dominant stable detected form was the complex of the 1:1 stoichiometry. However the stoichiometry changed depending on conditions. In order to assess more detailed the capacity of GSH/GSSG to interact with copper ions, competitive measurements were performed. In these assays, the indicator competes with GSH/GSSG for the chelated metal. Mild competetive assay with hematoxylin suggested the formation of 1:1 complex with GSSG and 1:2 with GSH (metal to glutathione). More competetive assay with bathocuproin showed that GSH complex was not stable, while that of GSSG was stable only in very high ratios, GSSG to Cun+. The reduction ability of GSH seemed to be responsible for this phenomenon.

CONCLUSIONS:

This study showed that glutathione in both reduced (GSH) and oxidized (GSSG) forms are the chelators of copper ions.

ACKNOWLEDGEMENTS:

This study was supported by Czech Science Foundation (18-00121S).

REFERENCES:

1. Anderson ME (1998). Chem Biol Interact, 111-112:1-14.
2. Aliaga ME, López Alarcón C, Bridi R, Speisky H (2016). J Inorg Biochem, 154:78-88.
3. Job P. Annali di Chimica (1928). 9:113-134.
4. Filipsky, T, Riha M, Hrdina R, Vavrova K, Mladenka (2013). Bioorg. Chem., 49:1-8

P-126: THE EFFECT OF CARVEDILOL TREATMENT ON ERECTILE DYSFUNCTION IN STREPTOZOTOCIN INDUCED DIABETIC RATS.

[1,2] Yilmaz Oral, D., [2] Guven, B., [2] Kara, Z., [2] Gur, S., [2] Onay Besikci, A.

[1] Cukurova University, Department of.Pharmacology, Adana, Turkey

[2] Ankara University, Department of Pharmacology, Ankara, Turkey

INTRODUCTION:

Diabetes is associated with an increased risk of erectile dysfunction (ED). Diabetic men having problems with achieving and/or maintaining an erection could take phosphodiesterase type 5 inhibitors as first-line therapy. A nonselective β blocker, carvedilol, inhibits β-1 and β-2 adrenergic as well as α-1 adrenergic receptors, thereby causes vasodilation (1). In addition, carvedilol has been shown to improve the heart rate variability and systolic blood flow in cavernous and dorsal arteries in patients with arterial hypertension (2). The present study aimed to evaluate the effect of carvedilol treatment on ED in streptozotocin (STZ)-induced diabetic rats.

MATERIALS AND METHODS:

Thirty adult male Sprague-Dawley rats were divided into four groups: 1) Control, 2) carvedilol (orally, 10mg/kg/day, 4-week)-treated control, 3) STZ (40 mg/kg, i.p., 8-week)-induced diabetic and 3) carvedilol-treated diabetic rats. Carvedilol was given after 8-week of diabetes. The relaxation and contraction responses of corpus cavernosum (CC) were examined after 12 weeks in organ bath studies.

RESULTS:

The carvedilol treatment had no effect on body weight and blood glucose in diabetic rats. In organ bath studies, endothelium-dependent acetylcholine relaxation of corpus cavernosum was significantly decreased in the diabetic group. However, no improvement was observed after carvedilol treatment. Surprisingly, neurogenic relaxation responses were significantly diminished in the cavernosal tissues of diabetic rats (15.6±5.0, $p<0.01$) which was normalized by the treatment (58.9±9.3). The relaxation response to sodium nitroprusside, a nitric oxide donor, was not changed in the groups. Furthermore, decreased relaxation responses to sildenafil, phosphodiesterase type 5 inhibitor, at 10μM dose in diabetic rats (diabetic, 22.6±2.4; control 45.8±3.8, $p<0.05$) were ameliorated after carvedilol treatment (47.9±5.0). Neurogenic (25.9±2.6, $p<0.01$) and phenylephrine (22.0±2.4, $p<0.01$) contractile responses in the diabetic group were lower than in the control group (51.4±7.5 and 54.7±5.3), which was restored after the treatment (45.6±3.4 and 65.0±6.1, respectively).

CONCLUSIONS:

Our data demonstrate that the carvedilol treatment is likely to improve the activity of neurogenic relaxation and contraction response as well as the relaxation response to phosphodiesterase type 5 inhibitor in erectile tissue of diabetic rats. Carvedilol may be a useful candidate for ED in diabetic men who have a potential risk of cardiovascular diseases. Further studies could help to confirm these findings and clarify the effect of combined treatment with carvedilol and phosphodiesterase type 5 inhibitors on diabetes-induced ED.

REFERENCES:

1. Feuerstein GZ, Ruffolo RR Jr (1996). Eur Heart J., Apr;17 Suppl B:24-9.
2. Mustafaev II, Nurmamedova GS (2013). Kardiologiia, 53(2):48-54.

P-127: THE POSSIBLE BENEFICIAL EFFECT OF IVABRADINE TREATMENT ON ERECTILE TISSUE IN A DIABETIC RAT MODEL

[1,2] Yilmaz Oral, D., [2] Kara, Z., [2] Guven, B.,[2] Onay Besikci, A., [2] Gur, S.

[1] Cukurova University, Department of.Pharmacology, Adana, Turkey

[2] Ankara University, Department of Pharmacology, Ankara, Turkey

INTRODUCTION:

Erectile dysfunction (ED) worsening in diabetic men with heart failure is not surprising as the endothelial dysfunction is a pathophysiologic sign of diabetes. Ivabradine, a selective inhibitor of the If channel and used for the treatment of heart failure, can improve the endothelial function in mice with hypercholesterolemia (1). The present study aimed to determine the effect of ivabradine treatment on ED in streptozotocin (STZ)-induced diabetic rats.

MATERIALS AND METHODS:

Thirty adult male Sprague-Dawley rats were divided into four groups: 1) Control, 2) ivabradine (orally, 10mg/kg/day, 4-week)-treated control, 3) STZ (40 mg/kg, i.p., 8-week)-induced diabetic and 4) ivabradine-treated diabetic rats. Ivabradine was given after 8-week of diabetes. Corpus cavernous (CC) responses were evaluated after 12 weeks.

RESULTS:

Treatment with ivabradine had no effect on blood glucose in diabetic rats. In organ bath studies, endothelium-dependent acetylcholine relaxation of corpus cavernosum was significantly decreased in the diabetic group (18.0±2.4, $p<0.01$) which was further restored after ivabradine treatment (43.4±7.5). In addition, neurogenic relaxation responses were

significantly reduced in the cavernosal tissues of diabetic rats (17.0±5.7, p<0.001) which was improved by the treatment (55.0±7.1). The relaxation response to nitric oxide donor, sodium nitroprusside, was not altered in groups. However, relaxantion response to phosphodiesterase type 5 inhibitor, sildenafil, was increased after ivabradine treatment in diabetic rats. However, the maximum relaxation response to sildenafil was not changed in groups. Contractile responses were significantly attenuated in the diabetic group which was normalized after the treatment.

CONCLUSIONS:

These results indicate that mechanism of action of ivabradine treatment may involve the cooperative activity of endothelial and neurogenic erectile response in corpus cavernosum in diabetic rats. Further studies could help to identify the molecular mechanisms underlying the beneficial effect of ivabradine treatment on diabetic ED.

REFERENCES:

1. Baumhäkel M, Custodis F, Schlimmer N, Laufs U, Böhm M (2010). Atherosclerosis, 212(1):55-62.

P-128: ANTI-NOCICEPTIVE ACTIVITIES OF SOME THIADIAZOLE DERIVATIVES

Eker, D., Ucel, UI., Can, OD., Ozkay Demir, U.

[1]Anadolu University, Department of Pharmacology, Eskişehir, Turkey

INTRODUCTION:

Thiadiazole is an important pharmacophore group frequently used in the drug development studies (1). Various thiadiazole derivatives have been reported for many different pharmacological effects, so far (2,3). One of the well-known activity induced by these derivatives is analgesia. Previous studies indicated that both of central and peripheral mechanisms may mediate the anti-nociceptive effects of these derivatives. Therefore, in the present study, we aimed to investigate possible anti-nociceptive activities of some thiadiazole derivative compounds.

MATERIALS AND METHODS:

Male CD1 mice, weighing 30-35 g, were used for the tests. Possible anti-nociceptive effect of the test compounds (30 mg/kg, i.p) on thermal, mechanical, and chemical nociceptive pathways were assessed by hot-plate, tail-clip and acetic acid induced writhing tests, respectively. Besides, assessment of motor coordination was carried out using Rota-Rod test. The experimental protocol of this study was approved by the Anadolu University Animal Experiments Local Ethics Committee.

RESULTS:

Compounds 2c, 2d, 2e, 2f, 2g and 2h increased the reaction time of animals recorded in hot-plate and tail-clip tests, indicating the centrally mediated anti-nociceptive activities of these derivatives. Besides, compounds 2e and 2f decreased the total number of writhing behaviors in the acetic acid induced writhing test suggesting that peripheral mechanisms are also contributed the anti-nociceptive activities of these compounds, as well as central ones. None of the tested compounds changed the falling latencies of mice in the Rota-rod tests, so the exhibited anti-nociceptive activities are specific.

CONCLUSIONS:

Among the tested thiadiazole derivatives, compounds 2c, 2d, 2e, 2f, 2g and 2h have significant anti-nociceptive activities. However, further clinical studies are needed to clarify their potentials as analgesic drug candidates.

ACKNOWLEDGEMENTS:

Authors of the study thanks to Assoc. Prof. Dr. Yusuf Ozkay for his supports in the synthesis studies.

REFERENCES:

1. Siddiqui et al., (2009). Journal of Chemical and Pharmaceutical Research, 1:19-30.
2. Pattanayak et al., (2009). Medicinal Chemistry Research, 18:351-361.
3. Sharma et al., (2011). Medicinal Chemistry Research, 20:245-253.

P-129: A RISK ASSESSMENT OF FEBRILE NEUTROPENIA IN AN ONCOLOGY OUTPATIENT CLINIC

[1] Aras, E., [1] Ozdemir, N., [1] Tecen Yucel, K., [1] Bayraktar Ekincioglu, A., [2] Kilickap, S.

[1] Hacettepe University, Faculty of Pharmacy, Department of Clinical Pharmacy, Ankara-Turkey

[2] Hacettepe Cancer Institute, Department of Medical Oncology, Ankara-Turkey

INTRODUCTION:

Febrile neutropenia (FN) is a serious complication of myelosuppressive therapy, which can lead to reduction in dose and/or termination of chemotherapy. The use of granulocyte colony-stimulating factor (G-CSF) reduces the severity and duration of FN. An initiation of G-CSF treatment in patients receiving chemotherapy protocols with a risk of developing FN ≥20% for primary prophylaxis is strongly recommended. In chemotherapy protocols where the risk of FN is 10-20%, the G-CSF treatment should be initiated if patients have identified risk factors. Therefore, aim of this study was to assess the pattern of G-CSF use by the Patient Risk Score (PRS)1 in oncology outpatients.

MATERIALS AND METHODS:

This prospective, cross-sectional study was conducted at the Hacettepe University Oncology

Hospital outpatient clinic between April-August 2017. The risk assessment for FN was undertaken on each cycle of chemotherapy by a clinical pharmacist at the clinic by using PRS. The patients who are ≥18 years of age and receive a chemotherapy protocol of developing FN risk is 10-20% and >20% were included and followed for 3 months during the study.

RESULTS:

A total of 118 patients (50% female) were included in the study; 49 and 67 patients use lenograstim and filgrastim, respectively. Among those, 69 (58.5%) patients used G-CSF for primary prophylaxis and 49 (41.5%) for secondary prophylaxis. Lenograstim was the most commonly used drug for primary prophylaxis. Although the risk of developing FN at the initial visit (PRS <3) was low in 45 (38.5%) patients, they were initiated to use G-CSF treatment. There were no significant differences in PRS values of patients on each cycle during 3 months follow-up (p>0.05).

CONCLUSIONS:

Although no statistically significant difference was found in the assessment of PRS values, it is important to assess patients individually in terms of risk of developing FN before each cycle during chemotherapy. PRS assessment can be used in a routine daily practice since it has easy-to-apply scoring systems and allows interpretation of risk factors individually.

ACKNOWLEDGEMENTS:

The authors would like to thank all participating patient and hospital staff at the outpatient clinic.

REFERENCES:

1. Gascón P, et al., (2016). Treatment patterns and outcomes in the prophylaxis of chemotherapy-induced (febrile) neutropenia with biosimilar filgrastim. Support Care Cancer, 2016;24:911-25.

P-130: PROTECTIVE EFFECTS OF A RIPK1 INHIBITOR, NECROSTATIN-1 ON CISPLATIN-INDUCED NEPHROTOXICITY IN RATS

[1] Erdinc, M., [1] Aslantas, M., [1] Uyar, E.,[1] Ozgen, ZE., [1] Kelle, I., [1] Akkoc, H., [2] Erdinc, L.

[1] Dicle University, Medical Faculty, Department of Medical Pharmacology, Diyarbakir, Turkey.

[2] Dicle University, Medical Faculty, Department of Biochemistry, Diyarbakir, Turkey.

INTRODUCTION:

Cisplatin (cis- diamminedichloroplatinum(II)) is a potent antineoplastic agent that is widely used to treat both adult and pediatric malignancies (1). The main dose-limiting side effect of cisplatin is its nephrotoxic effects (2). Clinical symptoms of cisplatin nephrotoxicity include; intense inflammatory response, injury in renal vasculature, reduced glomerular filtration and histopathologic abnormalities of acute tubular necrosis (3). Current literature suggests that necrostatin-1, a potent receptor-interacting serine/threonine-protein kinase 1 (RIPK1) inhibitor, prevents necroptosis through RIPK1 inhibition (4). This study aimed to investigate the protective effects of necrostatin-1 administration on cisplatin-induced nephrotoxicity in rats.

MATERIALS AND METHODS:

Male Wistar Albino rats weighted 250-350 gr were used in this study. Animals were separated into groups and treated with a single dose cisplatin (5 mg/kg; CIS) and necrostatin-1 (1,65 mg/kg/d for 5 days; NEC) or saline (%0.9) intraperitoneally (ip). Twenty hours after the injections, rats were sacrificed, and blood samples were collected to measure serum urea and blood creatinine levels. Left kidneys of rats were isolated and put on the Langendorff apparatus, perfused with Krebs solution to measure renal perfusion pressures. The right kidneys of rats were isolated to measure malondialdehyde (MDA) levels. The data were analyzed with Kruskal-Wallis Test, followed by Tukey's post hoc test if significant differences were detected.

RESULTS:

Blood serum urea levels were higher in CIS group ($p<0.01$) vs. control, and lower in CIS-NEC group ($p<0.01$) vs. CIS group. Serum creatinine levels were higher in CIS group ($p<0.01$) vs. control, and lower in CIS-NEC group ($p<0.01$) vs. CIS group. MDA levels were higher in CIS group ($p<0.01$) vs. control, and lower in CIS-NEC group ($p<0.05$) vs. CIS group. Renal perfusion pressures were higher in CIS group ($p<0.01$) vs. control, and lower in CIS-NEC group ($p<0.01$) vs. CIS group. NEC alone didn't alter renal perfusion pressures.

CONCLUSIONS:

Necrostatin-1, a RIPK1 inhibitor did successfully reduce cisplatin-induced nephrotoxic symptoms. To minimize the nephrotoxic side-effects of cisplatin treatment, necrostatin-1 appears as a promising supplementary agent to chemotherapy.

REFERENCES:

1. Florea AM et al., (2011). Cancers 3.1: 1351-1371.
2. Karimi G et al., (2010). Iranian Journal of Basic Medical Sciences, 13.2: 31.
3. Miller RP et al., (2010). Toxins 2.11: 2490-2518.
4. Xu X et al., (2010). Brain research, 1355: 189-194.

P-131: EVALUATION OF DRUG-DRUG INTERACTIONS ENCOUNTERED IN PEDIATRIC INFECTIOUS DISEASES UNIT

Polat, EC., Ozdemir, N., Bayraktar Ekincioglu, A., Demirkan, K.

Hacettepe University, Faculty of Pharmacy, Department of Clinical Pharmacy, Ankara, Turkey

INTRODUCTION:

Drug-drug interaction is described as an alteration of at least one drug's effect (such as increase, decrease or loss of effect) through various mechanisms where both drugs are administered concurrently. Drug-drug interaction leads to increase in morbidity and mortality, failure in treatment and also increase in health care expenditure indirectly. This study aimed to evaluate drug-drug interactions encountered in pediatric infectious diseases unit in a university hospital.

MATERIALS AND METHODS:

The study was conducted between 2nd-16th April 2018 at Hacettepe University Ihsan Dogramaci Children's Hospital Pediatric Infectious Diseases Unit. Patients' demographics and drug orders were collected by a clinical pharmacist through patients' medical records. Drug interactions were assessed on the first day of patient's drug order by using Micromedex® and Medscape online databases and the results were analyzed by IBM SPSS v.23.

RESULTS:

A total of 15 patients were included in the study. Of those, 80% were male (n=12), the mean (±standard deviation) age was 9.13 (±4.62) years and the number of drugs used per day was 5.53 (±2.5). A total of 14 drug interactions were identified by the Micromedex® and 55 interactions by the Medscape database. Among drug interactions identified by the Micromedex® (n=14); 7, 5 and 2 were categorized as major, moderate and minor interactions respectively. However, according to the Medscape, 5 (9.09%) interactions were indicated as contraindicated and serious, 16 (29.09%) as monitor closely and 34 (61.82%) as minor. Drug interactions were indicated as pharmacodynamic [19 (34.55%) and 12 (85.71%)] and pharmacokinetic [36 (65.45%) and 2 (14.29%)] by the Medscape and Micromedex, respectively. While the majority of the pharmacokinetic drug interactions identified by the Medscape were at absorption level (43.64%), interactions identified by the Micromedex® were predominantly pharmacodynamic (85.71%).

CONCLUSIONS:

The characteristics and management of drug interactions varies among interaction checker databases. Therefore, pharmacists should be aware of the mechanism of drug interactions, should compile scientific knowledge from various information sources then interpret them and provide appropriate strategies for its management.

P-132: EVALUATION OF POTENTIAL DRUG-DRUG INTERACTIONS AMONG PRESCRIPTIONS OF OUTPATIENTS FROM TRABZON, TURKEY

[1] Engin, S., [1] Barut, EN., [1] Eroglu, G., [2] Yaris, E., [1] Sezen, FS

[1] Karadeniz Technical University, Faculty of Pharmacy, Department of Pharmacology, Trabzon,Turkey

[2] Karadeniz Technical University, Faculty of Medicine, Department of.Pharmacology, Trabzon, Turkey

INTRODUCTION:

Drug-drug interactions (DDIs) defined as an altered response of one drug by cocurrent use of another drug is a major concern in polypharmacotherapy (1). Many studies based on primary care reports have revealed the prevalence for potential DDIs (pDDIs) ranging 12% to 80% (2). However, limited data is available about the prevalence of in outpatients in Turkey. The study was aimed to evaluate the prevalence and the severity of pDDIs in the prescriptions of outpatients from Trabzon.

MATERIALS AND METHODS:

A retrospective observational study was carried out and a total of 169 prescriptions from fifteen family practitioner centres were collected for a period of 4 months (February - May 2016) in Trabzon. Demografic information (age and gender), prescription details and the number of additional drug use were collected. pDDIs were checked by using the Drug Interactions Checker within the drugs.com database. Data were presented as mean±standart deviation or percentage of case. Independent sample t-test was used to assess differences among groups. The Pearson correlation coefficient was used to determine the relationship between two variables. $p<0.05$ was considered significant.

RESULTS:

A total of 169 prescription with mean age 42.10±25.20 years were analysed. The mean number of prescribed drugs per patient was 2.99±1.08. A total of 151 pDDIs were identified with mean of 0.89±1.83. Respiratory system drugs were the most frequently prescribed group (n = 78; 15.4 %). The prevalence of pDDIs was 39%. Acetylsalicylic acid was the most frequently prescribed drug involved in pDDIs (n=21, 13.9%), The most common pDDIs was Acetysalycilic acid with Metoprolol (n=4, 2.6%). Out of all pDDIs, 113 (74.8%) were of moderate, 27 (17.8%) were of minor, and 11(7.2%) were of major severity. The number of pDDIs are significantly correlated with age of the patients ($r=0.33$, $p<0.01$) and the number of prescribed drugs ($r=0.46$, $p<0.01$).

CONCLUSIONS:

Based on the study findings, the majority of interactions were moderate. Our results confirm the significant association of polypharmacy and age with the occurrence of pDDIs. Clinicians and pharmacists should be aware of the pDDIs to improve patient compliance and drug safety.

REFERENCES:

1. Juurlink DN, Mamdani M, et al., (2003). Drug–drug interactions among elderly patients hospitalized for drug toxicity. JAMA, 289:1652-8.
2. Teixeira JJV, Crozatti MTL, et al., (2012). Potential Drug-Drug Interactions in Prescriptions to Patients over 45 Years of Age in Primary Care, Southern Brazil. PLoS ONE, 7(10): e47062.

P-133: EFFECTS OF THREE DIFFERENT FLAVONOIDS ON CARDIAC CONTRACTILITY UNDER HIGH GLUCOSE CONCENTRATIONS

Kayki Mutlu, G., Yesilyurt, ZE., Erdogan, BR., Karaomerlioglu, I., Muderrisoglu, AE., Ari, N.

Ankara University, Faculty of Pharmacy, Department of Pharmacology, Ankara, Turkey

INTRODUCTION:

Hyperglycemia results in detrimental effects in heart including hypertrophy and functional abnormalities (1). On the other hand, dietary polyphenols are known to have preventive effects on the development of cardiac diseases (2). These polyphenols have been shown to regulate blood glucose leves and have protective effects in diabetes (3). Nevertheless, to our knowledge, their direct cardiac effect at the cellular level is not known. Thus, we aimed to investigate the effects of various polyphenolic substances from different classes under high glucose concentrations.

MATERIALS AND METHODS:

Ventricular cardiomyocytes were isolated from adult male Sprague–Dawley rats (300-400 g). Cells were treated with high glucose (25 μM) for 3 hours. Resveratrol, quercetin and apigenin was added 30 min prior to high glucose to a group of cells. A video-based edge detection system (IonOptix) was used to record changes in cell length during cell shortening and relengthening. *Cardiac contractility was assessed using peak shortening (PS) as an indicative of contractility, time to PS (TPS) as an indicative of systolic duration, time to* 90% relengthening (TR90) as an indicative of diastolic duration, maximal velocities of shortening/relengthening (± dL/dt) as indicatives of maximal velocities of ventricular pressure changes.

RESULTS:

Short term culture with high glucose concentrations elongated resting cell length. Moreover, those hyperglycemic cells showed decreased peak shortening (PS), speed of contraction and relaxation (± dL/dt). Resveratrol co-treatment improved these contractile parameters, however quercetin and apigenin did not.

CONCLUSIONS:

Resveratrol appears to improve cardiac parameters under hyperglycemia. However, quercetin and apigenin did not show any cardioprotective effects against hyperglycemia at the concentrations we used. Future studies using different polyphenolic substances are planned to be done.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Ankara University BAP (17B0237003).

REFERENCES:

1. Aloud BM, Raj P et al., (2016). Nutr Res., 36(2):134-42.
2. Yamagata K, Tagami M et al., (2015). Nutrition, 31(1):28-37.
3. Bahadoran Z, Mirmiran P et al., (2013). J Diabetes Metab Disord., 12:43.

P-134: RATIONAL DRUG USE IN THE MANAGEMENT OF HYPERTENSION AND THE ROLE OF THE COMMUNITY PHARMACIST

[1] Aylak, S., [2] Telli, G., [2] Tel, BC.,[2] Gumusel B.

[1] Turkiish Medıcınes And Medıcal Devıces Agency, Ankara, Turkey

[2] Hacettepe University, Department of.Pharmacology, Ankara, Turkey

INTRODUCTION:

Rational drug use (RDU) is described by World Health Organization as the administration of drugs at appropriate doses, using for sufficient time with the lowest cost for both patients and community (1). The correct explanation of effective use, side-effects and interactions of drugs to patients will prevent inappropriate usage of the drugs. Hypertension is one of the most common chronic disease in the world and the cost of the disease are increasing day by day with the aging of world population. RDU in the management hypertension will be reduced the cost of treatment. A multidisciplinary team-work and cooperation especially between doctor-pharmacist-patient require for a successful RDU. It was reported in many studies that in the treatment of hypertension, the blood pressure was controlled more effectively with the contribution of the community pharmacist (2). Therefore, informing the pharmacist about RDU is very important for the success of the treatment. The aim of this study is to assess the knowledge of the community pharmacist and the information that were

provided to patients about the drugs in hypertension treatment in Greater Ankara area.

MATERIALS AND METHODS:

A survey was applied to 110 pharmacists who were accepted to participate the study.

RESULTS:

According to survey, 1.8% of the pharmacists reported that the prescription of hypertension treatment was dispensed rarely, 9.1% occasionally, 70% frequently and 19.1% contstantly. The pharmacists stated that, 35.5% of the participants were educated about rational use of hypertension drugs and 64.5% of them did not take an extra-education after graduation. The 88.1% of the pharmacists were reported that they informed the patient about lifestyle changes, 75.5% about the importance of the compliance to treatment and 87.2% informed the patients about the disease.

CONCLUSIONS:

These results underline the importance of the community pharmacist in the rational use of hypertension drugs. Therefore, raising awareness about RDU in the management of hypertension for the patients and pharmacists will provide significant benefits to public health and cost-effective drug use.

REFERENCES:

1. World Health Organization. The rational use of drugs. Report of the conference of experts. Nairobi, 1985.Book Chapter:
2. Cheema E, Sutcliffe P, Singer DJR (2014). Br J Clin Pharmacol, 78(6):1238-1247.

P-135: ULTRASTRUCTURAL INVESTIGATION OF THERAPEUTIC EFFECTS OF HUPERZINE-A ON OPTIC NERVE IN ALZHEIMER'S MODEL

[1] Bayrak, G., [2] Turkseven, CH., [3] Marasligil, B., [4] Dinc, E., [1] Balli, E., [2] Buyukakilli, B.

[1] Mersin University, Faculty of Medicine, Department of Histology and Embryology, Mersin, Turkey

[2] Mersin University, Faculty of Medicine, Department of Biophysics, Mersin, Turkey

[3] Mersin University, Faculty of Medicine, Department of Physiology, Mersin, Turkey

[4] Mersin University, Faculty of Medicine, Department of Ophthalmology, Mersin, Turkey

INTRODUCTION:

Alzheimer's disease (AD) is a chronic neurodegenerative disease which is characterized by the neuronal loss, cerebrovascular inflammation, the accumulation of amyloid plaques (Aβ) on the cerebral vessels and the brain parenchyma (1). It is known that estrogen replacement therapy may protect postmenopausal women from AD and help improve their cognitive function (2,3). Long-term intraperitoneal administration of D-gal can lead to oxidative stress, neuronal damage, and a decline in learning and memory capacity in rats (4). In the experimental AD model, female rats ovariectomized to avoid the protective effects of the estrogen and were injected intraperitoneal D-gal. In this study, we aimed to investigate the possible therapeutic effects of Huperzin-A (Hup-A) against the possible damage of the optic nerve in the ovariectomized experimental AD model with ultrastructurally.

MATERIALS AND METHODS:

Sixty-eight female Sprague-Dawley rats were divided control, sham, ovariectomy, ovariectomy+D-galactose, ovariectomy+D-galactose+Hup-A groups. For the model of AD, D-galactose (i.p.) was administered at 100 mg/kg dose every day for 10 weeks ovariectomy+D-galactose and ovariectomy+D-galactose+Hup-A groups after the ovariectomy. At the end of the experiment, the rats were sacrificed and the removed optic nerves were examined with electron microscopy ultrastructurally.

RESULTS:

In the control, sham, and ovariectomy groups glial cells, myelinated and unmyelinated nerve fibers and perivascular areas were normal. Findings in the ovariectomy+D-galactose and ovariectomy+D-galactose+Hup-A groups were similar to the other groups.

CONCLUSIONS:

As a result of the study, it was determined that long-term D-galactose administration did not cause optic nerve damage after ovariectomy. In our next study, it is considered to improve the duration of D-galactose administration and / or dose and to reevaluate the possible effects on the optic nerve.

REFERENCES:

1. Zenaro E, et.al., (2017). The blood-brain barrier in Alzheimer's disease, Neurobiology of Disease, 107:41-56.
2. Dykens JA, et.al., (2005). Development of 17alpha-estradiol as a neuroprotective therapeutic agent: rationale and results from a phase 1 clinical study, Annals of the New York Academy of Sciences, 1052:116–135.
3. Feng Z, Cheng Y, et al., (2004). Long-term effects of melatonin or 17 betaestradiol on improving spatial memory performance in cognitively impaired, ovariectomized adult rats, Journal of Pineal Research, 37(3):198–206.
4. Hua X, et.al., (2007). Long-term D-galactose injection combined with ovariectomy serves as a new rodent model for Alzheimer's disease, Life Sciences 80:1897–1905.

P-136: EVALUATION OF THE QUALITY OF LIFE, ATTITUDES AND PERCEPTIONS IN PATIENTS WITH BENIGN PROSTATIC HYPERPLASIA

[1] Algorane, I., [1] Okuyan, B. [1] Sancar, M., [2] Cam, K.,[1] Izzettin, FV.

[1] Marmara University, Faculty of Pharmacy, Department of Clinical Pharmacy, Istanbul, Turkey

[2]Marmara University, Faculty of Medicine, Department of Urology, Istanbul, Turkey

INTRODUCTION:

The aim of our study is the evaluation of quality of life, illness perception, attitude toward medication of patients with benign prostatic hyperplasia in the urology outpatient department.

MATERIALS AND METHODS:

The study group was composed of seventy-four patients with benign prostatic hyperplasia over 40 years old. All patients were using at least one medication for BPH with a period of at least last 4 weeks. The following scales were used: 1.Morisky Green Levine Medication Adherence Scale to measure medication adherence, 2. Benign Prostatic Hyperplasia-Quality of Life Questionnaire to degree disease specific quality of life, 3.Brief Illness Perception Questionnaire and 4.Beliefs about Medicines Questionnaire (BMQ-T) to measure patients' perceptions of illness, treatment beliefs, and moods.

RESULTS:

The mean age of the participants were 64.86 ± 7.90 in the present study. Of them, 25.9% were defined as polypharmacy which is the use of five or more medication, out of 74 patients, 48 (64.9%) were adherent to their medication. The mean score of quality of life was 19.08±9.80 (2-44). The mean scores of BMQ-T for the necessity, concerns, harm, and overuse domains were 2.88±0.62, 3.47±0.71, 3.02±0.59, and 2.60±0.58, respectively. The mean score of brief illness perception was 39.72±13.41. There was significant correlation between the number of medication used and the score of specific concerns-BMQ-T ($r=0.328$, $p<0.05$). However, there was negative correlation between the number of medication used and the score of general overuse-BMQ-T ($r=-0.341$, $p<0.05$). There was a negative correlation between the scores of illness perception and specific concerns-BMQ-T ($r=-0.314$, $p<0.05$).

CONCLUSIONS:

According to our study results, the patients with BPH have moderate scores for brief illness perception and beliefs about medicines. Pharmacists could play an important role in patient education to improve their knowledge and perception regarding illness and medication in BPH.

P-137: ADHERENCE TO IMMUNOSUPPRESIVE MEDICATIONS IN RENAL TRANSPLANT PATIENTS.

Tecen Yucel, K., Aras, E., Ozdemir, N., Bayraktar Ekincioglu, A., Demirkan, K.

Hacettepe University, Department of Clinical Pharmacy, Ankara, Turkey

INTRODUCTION:

Patient adherence to immunosuppresive medication is one of the most important factor for the survival of a graft in transplant patients. The study aimed to assess patient adherence to immunosuppresive medications and factors that may affect adherence (1).

MATERIALS AND METHODS:

A prospective, observational study was conducted in a nephrology outpatient clinic at the Hacettepe University Hospitals between November 2017-February 2018. A clinical pharmacist was involved in clinic visits with specialist physicians and interviewed with patients who had transplantation, are taking tacrolimus, cyclosporine or everolimus and are willing to participate in the study. The data on patients' demographics and serum drug concentration were collected and the Immunosuppressive Therapy Adherence Scale (ITAS) at the clinic which consists of 4 questions (total score:12) was administered at the clinic. The patients with ITAS scores of 12 points were considered to have a perfect adherence. Factors that may affect adherence were evaluated by a logistic regression analysis.

RESULTS:

A total of 100 patients included in the study. The mean age (± standard deviation) was 39.73±1.20 and 56% were male. With regards to immunosuppressive medication; 67, 26 and 7 patients were using tacrolimus, cyclosporine and everolimus, respectively. Only 32 patients had ITAS score of 12 (perfect adherence), of those 22, 9 and 1 were on tacrolimus, cyclosporine and everolimus. A significant difference was found in serum drug concentration between patients who have ITAS score of 12 and score of ≤11 for patients taking tacrolimus ($p=0.022$). There were no statistically significant association established between patient adherence and factors such as age, body mass index, marital status, education level, number of additional diseases, number of medications used, pre-transplant dialysis history, transplantation type (cadaver/live), duration since transplantation, duration of immunosuppressive medication and thyroid stimulating hormone ($p>0.05$). Only a level of vitamin D was found to be a significant factor on adherence ($p=0.017$) where a unit increase has a positive effect on adherence [Odds Ratio (95% Confidence Interval): 0.819 (0.694-0.966)].

CONCLUSIONS:

Adherence to immunosuppressive medication in renal transplant patients is important. Healthcare professionals should be aware of the level of patient's adherence and its associated factors. A clinical pharmacist may play a critical role in identifying patient's level of adherence to maintain effective therapy.

ACKNOWLEDGEMENTS:

The authors would like to thank all participating patients and hospital staff at the outpatient clinic.

REFERENCES:

1. Little DJ, et al., (2016). Depression and Immunosuppressive Therapy Adherence Following Renal Transplantation in Military Healthcare System Beneficiaries. Kidney Int Rep;2(2):248-250.

P-140: A PROMISING SOLUTION FOR RHEUMATOID ARTHRITIS: CHARACTERIZATION, IN VITRO AND IN VIVO STUDIES

[1] Siafaka, P., [2] Okur, ME., [3] Ayla, S., [4] Karantas, I., [1] Ustundag Okur, N.

[1]Istanbul Medipol University, School of Pharmacy, Department of Pharmaceutical Technology, Istanbul, Turkey

[2]Anadolu University, Faculty of Pharmacy, Department of Pharmacology, Istanbul, Turkey

[3]Istanbul Medipol University, School of Medicine, Department of Histology and Embryology, Istanbul, Turkey

4Hippokration General Hospital, [2]nd Clinic of Internal Medicine, Thessaloniki, Greece

INTRODUCTION:

Rheumatoid arthritis is a progressive autoimmune disease which affects the functional ability and decrease the quality of life, due to polyarticular inflammation and joint damage. Leflunomide is a disease modified drug which is orally administered to be rapidly metabolized to active teriflunomide (TFL). TFL is responsible for its therapeutic action (1,2). The aim of this work was to evaluate the use of polymeric film containing two polymers, poly(ε-caprolactone) (PCL) and poly(butylene adipate) (PBAd) as a possible management of controlling the release of TFL from the product. Characterization, in vitro release and in vivo studies were performed.

MATERIALS AND METHODS:

PCL and PBAd were prepared as previously reported (2). PCL/PBAd patches were developed via solvent evaporation technique, by using dichloromethane (DCM). Immiscible PCL/PBAd blends were produced by dissolving the polymers to DCM until full solvent evaporation. 90/10, 70/30 and 50/50 were loaded with 5, 10 and 15 wt% TFL. In vitro degradation rate using Simulated Body Fluid ruled out increased hydrolysis. A skin irritation experiment was done with healthy BALB-c mice. Mice were divided into four groups (saline (SP), TFL loaded blends (70/30 and 50/50), and TFL loaded suspension).

RESULTS:

Compatibility studies between drug and polymeric blends as conducted via FTIR, XRD and SEM analysis exhibited amorphization of the drug into the matrix which led to improved solubility of the drug (Fig 1). In vitro release showed the expected high dissolution rate which it was time dependent and associated with the hydrolysis degradation (1,2). In further, histopathology studies manifest the safety of the above patches claiming that TFL loaded PCL/PBAd blends are appropriate vehicles for the dermal application of TFL (Fig 1c).

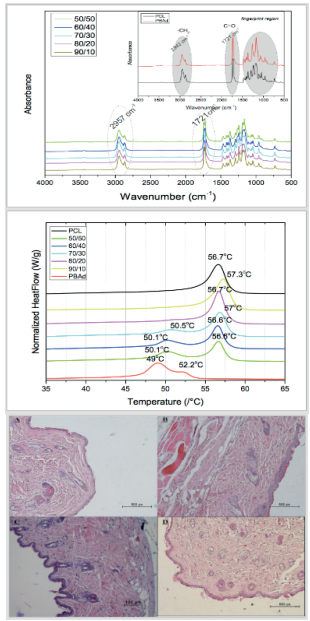


Fig 1. a) FT-IR and b)DSC studies of PCL and PBAd blends c) Images of treated mice skin with a)70/30+5% TFL, b)with 50/50+5% TFL, c)with SP and d)with 5% TFL suspension.

CONCLUSIONS:

It can be concluded that the prepared carriers are quite promising for patients since they can limit the side effects rising from TFL drug.

ACKNOWLEDGEMENTS:

The authors would like to acknowledge Istanbul Medipol University MEDITAM.

REFERENCES:

1. Siafaka P, Barmbalexis P, Bikiaris D (2016). Eur J Pharm Sci, 88:12-25.
2. Siafaka P et al., (2015). Eur J Pharm Biopharm, 94:473-484.

P-141: INCREASED ANTILEUKEMIC EFFECTS IN HUMAN CHRONIC MYELOID LEUKEMIA BY COMBINING EVEROLIMUS AND SUNITINIB

[1] Ergul, M., [2] Ergul, M., [3] Terzi, H., [4] Altun, A.

[1]Cumhuriyet University, Department of Pharmacology, Sivas, Turkey

[2]Cumhuriyet University, Department of Biochemistry, Sivas, Turkey

[3]Cumhuriyet University, Department of Hematology, Sivas, Turkey

4Cumhuriyet University, Department of Medical Pharmacology, Sivas, Turkey

INTRODUCTION:

Sunitinib is a multitargeted receptor tyrosine kinase inhibitor with selectivity against PDGFR and VEGFRs, approved for treatment of patients with advanced renal cell cancer. Furthermore, sunitinib has been shown to be active against acute myeloid leukemia (AML) cells in vitro and in vivo, and the synergistic growth inhibition of these cells occurred when sunitinib was combined with the conventional anticancer agents (1). The serine/threonine kinase mammalian target of rapamycin (mTOR) is activated by phosphatidylinositol 3-kinase/Akt signaling and regulates cell proliferation. The mTOR inhibitors, rapamycin or its analogue everolimus (RAD001), have been shown to be active against many types of solid tumors, as well as subsets of leukemia, and are now being used in clinical trials (2). The present study aimed to determine whether everolimus can enhance anticancer effect to sunitinib; for this purpose the combined effects of everolimus with sunitinib on K562 cells were investigated.

MATERIALS AND METHODS:

K562 cells were cultured and treated with different concentrations (100, 10, 1, 0.1, 0.01 μM) of everolimus/sunitinib alone and everolimus in combination with sunitinib. The cell viability was determined by 2,3-bis (2-methoxy-4-nitro-5-sulfophenyl)-2-tetrazolium 5-carboxanilide (XTT) cell proliferation assay.

RESULTS:

Our results showed that everolimus, sunitinib and everolimus-sunitinib combination exposure inhibited K562 cell proliferation ($p<0.05$) in a dose-dependent manner compared to the control cells. The IC50 of everolimus, sunitinib and everolimus-sunitinib combination in K562 cell line were calculated as 73 μM, 91 μM and 51 μM after 24 h of treatment, respectively.

CONCLUSIONS:

In conclusion, our cytotoxicity results revealed that the everolimus-sunitinib combination is more toxic than sunitinib alone on K562 cells. Taken together, sunitinib may be useful for the treatment of individuals with leukemias possessing activating mutations in RTK; and the combination of sunitinib and everolimus represents a promising novel treatment strategy.

REFERENCES:

1. Yee KW, Schittenhelm M, O'Farrell AM et al., (2004). Blood, 104:4202-9.
2. Chan S (2004). Br J Cancer, 91:1420-4.

P-142: EVALUATION OF IN VITRO ANTICANCER ACTIVITY OF VERONICA OFFICINALIS LEAVES EXTRACTS ON BREAST CANCER CELLS MDA-MB-231.

[1] Ergul, M., [2] Ergul, M., [3] Eruygur, N.

[1]Cumhuriyet University, Department of Pharmacology, Sivas, Turkey

[2]Cumhuriyet University,Department of Biochemistry, Sivas, Turkey

[3]Selçuk University, Faculty of Pharmacy, Department of Pharmacognosy, Konya, Turkey

INTRODUCTION:

Veronica officinalis (V. officinalis) is a widespread species found growing long forest edges, in underwood and meadows up to subalpine altitudes (1, 2). Especially in the 16th and 17th centuries, V. officinalis was recommended for stomach and intestinal diseases, renal lithiasis, pulmonary diseases and colic (3). The present study aimed to evaluate the anti-proliferative effect of the methanol and water extracts of V. officinalis leaves on MDA-MB-231 cells.

MATERIALS AND METHODS:

MDA-MB-231 and L929 cell lines were cultured and treated with different concentrations (0.0625, 0.125, 0.25, 0.5, 1 mg/mL) of V. officinalis for 24 h. 2,3-bis (2-methoxy-4-nitro-5-sulfophenyl)-2-tetrazolium 5-carboxanilide (XTT) cell proliferation assay was used to evaluate the antiproliferative effects of the water and methanolic extracts of V. officinalis leaves on MDA-MB-231. L929 cell lines were also used as healthy control cells.

RESULTS:

The methanol extract of V. officinalis significantly inhibited MDA-MB-231 cell proliferation ($p<0.05$) at 0.25-1 mg/mL concentration range in a dose-dependent manner. However, the water extract of V. officinalis exhibited important anticancer activity ($p<0.05$) at 0.5-1 mg/mL concentrations in a dose-dependent manner. The IC50 values of the water and methanol extracts of V. officinalis in MDA-MB-231 cell line was calculated as 0.092 mg/mL and 0.45 mg/mL after 24 h of treatment, respectively. However, neither extract showed any significant cytotoxicity on the L929 cell line at the concentration range (0.0625-1 mg/mL).

CONCLUSIONS:

According to the experimental results the methanol extract of V. officinalis exhibited more significant anticancer activity than the water extract on MDA-MB-231 cells. This may be due to the fact that the methanol extract has richer active ingredients than the water extract. Consequently, the methanolic extract of V. officinalis leaf may be considered as a potential therapeutic agent in cancer.

REFERENCES:

1. Flora R.P.R (1960). vol.VII,Ed.Acad.R.P.R., Bucharest, p.536.
2. Gründemann C et al., (2013). Journal of Ethnopharmacology, 145, 118-126.
3. Scarlat M, Sandor V, Tamas M, Cuparencu B (1985). Journal of Ethnopharmacology, 13,157-163.

P-143: A COMPARISON OF THE ANTIOXIDANT PROPERTIES OF FLUOXETINE AND MELATONIN IN MICE BRAIN TISSUE

[1] Erdinc, M., [1] Inci Camci, M., [1] Uyar, E., [1] Kelle,I., [1] Akkoc, H., [2] Erdinc, L.

[1]Dicle University, Medical Faculty, Department of Pharmacology, Diyarbakır, Turkey

[2] Dicle University, Medical Faculty, Department of Biochemistry, Diyarbakır, Turkey

INTRODUCTION:

During exposure to stress, neurochemical, hormonal and behavioral changes occur in the body(1). Studies revealed that subchronic stress application is related to oxidative stress and it increases lipid peroxidation, nitrite levels, catalase activity and decreases glutathione levels in the brain(2).In various studies, it is stated that melatonin is a useful agent to prevent oxidative damage arisen from stress with various mechanisms(3). Fluoxetine, on the other hand, has shown therapeutic benefits in the protection of the brain cells against oxidative damage and the prevention of depression and anxiety due to reduced serotonergic activity during stres(4). This study aimed to investigate the antioxidant effects of fluoxetine, melatonin and their combinations on subchronic immobilization-induced stress in mice.

MATERIALS AND METHODS:

BALB/c mice weighted 30-40 gr were separated into groups and either treated intraperitoneally (ip) with melatonin (10 mg/kg, Mel), fluoxetine (20 mg/kg, Flu) for 7 days or had %0.9 saline injections. Immobilization (IM) groups were placed into individual cages 6 hours for 7 days. Mice were sacrificed by decapitation to assess malondialdehyde (MDA) levels. The results were evaluated using One-way ANOVA followed by Kruskal-Wallis test. Data are presented as mean and ±SEM.

RESULTS:

The measured MDA levels in the immobilization applied mice group brain tissue samples were significantly higher than those of the control group ($p<0.01$). Melatonin, fluoxetine and their combination did decrease the increased MDA levels to normal levels.

CONCLUSIONS:

In this study, melatonin has been found as effective as fluoxetine in reducing oxidative damage induced by stress application. Secreted endogenously or taken as exogenous medication, melatonin could pose a remarkable alternative to fluoxetine, which has disturbing side effects. Further studies should be conducted to reveal beneficial effects of melatonin in various physiological and psychiatric disorders.

ACKNOWLEDGEMENTS:

This study was supported by a grant of DUBAP (TIP.16.011)

REFERENCES:

1. Dhir A, Padi SS, Naidu PS, Kulkarni SK (2006). Eur J Pharmacol, 535:192-198.
2. Sahin E, Gumuslu S (2007). Comp Biochem Physiol C Toxicol Pharmacol, 144:342-347.
3. Ali T, Badshah H, Kim TH, Kim MO (2015). J Pineal Res, 58:71-85.
4. David DJ, Samuels BA, Rainer Q, Wang JW, Marsteller D, Mendez I, et al., (2009). Neuron, 62:479-493.

P-144: HEPATOPROTECTIVE EFFECT OF GENTIANA OLIVIERI ON CHRONIC UNPREDICTABLE STRESS MODEL OF DEPRESSION IN THE RATS

[1] Berk, A., [2] Kaymaz, MB., [2] Yilmaz, I., [3] Abacioglu, N.

[1] The Health Sciences University Elazig Training and Research Hospital, Department of Pharmacy, Elazig, Turkey

[2] Inonu University, Department of Pharmacology, Malatya, Turkey,

[3] Near East University, Department of Pharmacology, Nicosia, North Cyprus

INTRODUCTION:

Flowering herbs of Gentiana olivieri known with a local name as “Afat”, is traditionally been used in south-east Anatolia as bitter tonic, stomachic and to combat some mental disorders including depression in the different regions of Turkey (1). Studies have consistently showed associations between depression and liver diseases and also antidepressant drugs can cause drug-induced liver injury (2, 3). The aim of this

study is to investigate the hepatoprotective effect of G. olivieri in different doses on chronic unpredictable stress (CUS) induced depression and to compare the results with imipramine.

MATERIALS AND METHODS:

72 male Sprague dawley rats were were divided into 9 groups (8 animals in each group) and were subjected to an experimental setting of CUS procedure according to the method of Muscat et al (1990) (4). The animals were orally administered imipramine (10 mg/kg), the ethanol extract of G. olivieri (1000 mg/kg, 500 mg/kg and 200 mg/kg) alone and in combination of imipramine (10 mg /kg) for 21 days on CUS model of depression. CUS-induced liver injury was examined by measuring liver TBARS, GSH and SOD levels.

RESULTS:

CUS-induced depression increased liver TBARS level ($p<0,001$), reduced liver GSH and SOD levels ($p<0,01$). G. olivieri reversed CUS-induced impairment in liver antioxidant by decreasing TBARS level ($p<0,01$) and increasing GSH and SOD levels ($p<0,01$) at 1000 mg/kg dose; decreasing TBARS level ($p<0,01$) and increasing GSH level ($p<0,05$) at 500 mg/kg dose and decreasing TBARS level at 200 mg/kg dose ($p<0,05$). 10 mg/kg imipramine did not alter these parameters significantly. G. olivieri when used in combination of impramine also produced beneficial effect by decreasing TBARS level ($p<0,01$) and increasing GSH and SOD levels ($p<0,001$) at 1000 mg/kg dose; decreasing TBARS level ($p<0,001$) and increasing GSH and SOD levels ($p<0,001$) at 500 mg/kg dose; decreasing TBARS level ($p<0,05$) and increasing GSH level ($p<0,05$) at 200 mg/kg dose.

CONCLUSIONS:

G. olivieri may be beneficial for stress induced impairment in liver and may reduce the side effects of synthetic antidepressants such as imipramine related to liver. Further investigations are needed on the potential use of G. olivieri in clinical depression.

ACKNOWLEDGEMENTS:

This work was supported by İnönü University, Scientific Research Project (BAP), (Project No:2015/36).

REFERENCES:

1. Sezik E, Aslan M et al., (2005). Life sciences, 76(11):1223-38.
2. Voican CS, Corruble E et al., (2014). The American journal of psychiatry, 171(4):404-15.
3. Patten SB, Williams JV et al., (2008). General hospital psychiatry, 30(5):407-13.
4. Muscat R, Sampson D et al., (1990). Biological psychiatry, 28(3):223-30.

P-145: EFFECTS OF COTINUS COGGYGRIA LEAF EXTRACT AND PHENYTOIN ON BURN WOUNDS

Kaymaz, MB., Berk, A., Aktay, G.

Inonu University, Department of Pharmacology, Malatya, Turkey

INTRODUCTION:

Healing of burn wounds, managed by many cytokines and mediators in which inflammation and hypermetabolism are seen. Superficial burns can be treated with topical pharmaceutical forms (1). This study aimed to examine the effects of methanolic leaf extracts of Cotinus coggygria plant that grows in our country, and phenytoin, an antiepileptic drug, on an experimental 2nd degree burn wound.

MATERIALS AND METHODS:

Sprague-Dawley rats (n=40) were divided into 5 groups and 2nd degree burns were induced on the shaved backs by pressing a heated (100ºC) copper plate (3x4 cm) for 5 seconds according to the Khodja et al. method (2). Groups were constituted as Control (base ointment), Silverdin®, 1% methanolic C.coggygria extract, 2% Phenytoin, 1% C.coggygria + 2% Phenytoin. For treatment, 0.5 g of ointment was applied to the burned areas for 14 days. The blood samples were analyzed for the levels of neopterin and interleukin-6. The tissue levels of some parameters related to oxidative stress such as lipid peroxidation (TBARs), glutathione (GSH), total thiol groups (T-SH) as well as hydroxypyroline and caspase-3 were determined. Digital photographs were taken on 3rd, 7th and 14th days to examine the prognosis of the wounds. The burned areas were standardized using Cam-Scanner and Photoshop software, compared in terms of number of pixels. One-way analysis of variance (ANOVA) and Tukey's test were used to compare the groups with the control group.

RESULTS:

In the Cotinus group, statistically significant differences compared to controls were found in terms of TBARs ($p<0.001$) and other parameters ($p<0.05$) except for neopterin. Phenytoin significantly improved all parameters ($p<0.001$), In the Cotinus+Phenytoin group, significant results were obtained in all parameters ($p<0.05$ and $p<0.01$). The sizes of the wounds were markedly reduced in the Cotinus ($p<0.05$) and phenytoin ($p<0.001$) group compared to the control on 14th day.

CONCLUSIONS:

C.coggygria plant significantly contributes to healing possibly by means of the main component of its methanolic extract that possesses strong antioxidant and anti-inflammatory capabilities, i.e gallic acid (3). Phenytoin may have strengthened the connective

tissue by means of its epithelizing effect. Combined administration of Cotinus and phenytoin may have synergistic effect especially on GSH that forms the antioxidant defense pool. Since the sizes of the wound areas tend to reduce, it could be suggested that this is a promising preparation which may contribute to the treatment of burn wounds.

REFERENCES:

1. Nisancı M, Ozturk S (2010). J Plast Surg-Special Topics, 2(1):8-14.
2. Khodja AN, Mahlous M et al., (2013). Burns, 39:98-104.
3. Matic S, Stanic S et al., (2016). Saudi Journal of Biological Sciences, 23(4):452-461.

P-146: THE EFFECT OF PREGABALIN ON ELECTROCONVULSIVE THERAPY

Yalcin, N., Kelleci Cakir, B., Surmelioglu, N., Celiker, A., Bayraktar Ekincioglu, A., Demirkan K.

Hacettepe University, Faculty of Pharmacy, Department of Clinical Pharmacy, Ankara, Turkey

INTRODUCTION

Electroconvulsive therapy (ECT), with external electrical stimulation; Triggering epileptic grand mal epileptic seizures for treatment in patients with high suicide risk, not responding to antidepressant drugs, in situations where drug use is high risk, such as pregnancy / lactation, in patients with severe mania, schizophrenia, schizoaffective disorder. Studies shown that, in severe depression situations, it has a positive effect and limited side effects in a short time. The treatment may be administered in a total of 12-20 sessions, twice a week; This number varies according to the clinical response of the patient. After acute treatment, maintenance treatment is started when necessary.

MATERIALS AND METHODS

Effect of concurrent administration of ECT with pregabalin which is one of the antiepileptic drugs on seizure threshold and duration was intended to shown.

RESULTS

A 38-year-old, married, 1 child-admitted male patient was admitted to the hospital with alcohol and benzodiazepine dependence and depression.

The patient uses risperidone 2mg, fluoxetine 40mg, pregabalin 300mg, clonazepam 4mg and vitamin B complex. It was first decided in 1998 that the patient diagnosed with depression had started ECT on the patient after the depressive episodes had increased in the last two years.

When the patient receives the first ECT, the target energy-induced seizure is not achieved with the applied energy. Therefore, because of the failure with the energy applied for the first seizure patient need an increased dose of energy at the same day and the application was repeated once more, but couldn't achieved an effective result. Clinical pharmacist was found that the condition of inability to achieve the desired treatment of seizures due to concomitant use of pregabalin. Pregabalin an anticonvulsant drug that affects the threshold and duration of seizures. Clinical pharmacist suggest that in the next ECT session pregabalin dose should be reduced half of the normal dose. In the second session of the treatment, the targeted active attack is provided with the applied energy. The patient's treatment was terminated successfully and ECT applied 12 sessions in total.

CONCLUSIONS

Due to the prevalence of seizure threshold and duration in patients who are scheduled to undergo ECT is critical, the medications used by the patient should be evaluated with a multidisciplinary team before to initiate for ECT treatment.

REFERENCES

1. Zolezzi M (2016). Neuropsychiatric disease and treatment, 12:931.
2. Nitturkar AR et al, (2016). Indian journal of psychiatry, 58.2:190.

P-147: CONTRIBUTION OF DELTA OPIOID RECEPTORS TO ANTI-HYPERALGESIC EFFICACY OF REBOXETINE

Turan Yucel, N., Demir Ozkay, U., Can, OD.

Anadolu University, Department of Pharmacology, Eskisehir, Turkey

INTRODUCTION:

Reboxetine is a potent and selective noradrenaline re-uptake inhibitor prescribed for the treatment of major depression in many countries. We have recently reported the anti-hyperalgesic and anti-allodinic effects of reboxetine in diabetic rats. We also have demonstrated the contribution of dopaminergic system to these effects. Based on the role of delta opioid receptors (δOR) in the processes related to pain (1-3), in this study, we planned to investigate the possible involvement of δOR in the anti-hyperalgesic effect of reboxetine in order to provide further mechanistic approach for the mode of action.

MATERIALS AND METHODS:

Male Sprague-Dawley rats (250-300 g) were used for the experiments. Diabetes was induced by a single i.v. injection of streptozotocin (STZ, 50 mg/kg). Reboxetine (8 mg/kg/day, p.o.) treatment was started after 4-week diabetic period which is required for neuropathy development. After 2 weeks treatment period, mechanical and thermal hyperalgesia were assessed using the Randall-Selitto and Hargreave's

tests, respectively. Potential involvement of the δOR in the pharmacological effect of the reboxetine was assessed using naltrindole (a δOR antagonist, 3 mg/kg, i.p.). The experimental protocol of this study was approved by the Local Ethical Committee of Anadolu University.

RESULTS:

Subacute administration of reboxetine for 2 weeks induced a significant increase in the declined paw-withdrawal thresholds of diabetic rats in the Randall-Selitto tests. Similarly, reduced paw-withdrawal latencies of diabetic rats in Hargreave's tests were significantly prolonged by reboxetine. Moreover, the observed anti-hyperalgesic activity of this drug against mechanical and thermal nociceptive stimuli was antagonized by naltrindole pre-treatment.

CONCLUSIONS:

The results suggest that δOR subtype plays a role in the anti-hyperalgesic activity of reboxetine. However, the contribution of the opioid system to this pharmacological activity should be further clarified.

ACKNOWLEDGEMENTS:

This work was supported by a grant of Research Foundation of Anadolu University (1606S549).

REFERENCES:

1. Holdridge SV, Cahill CM (2007). European Journal of Pain, 11:685-693.
2. Castany et al., (2016). Neuroscience Letters, 614:49-54.
3. McDonnell et al., (2017). PLoS One, 12:e0180998.

P-148: ANTIDEPRESSANT-LIKE EFFECT OF SOME BENZIMIDAZOLE-PIPERIDINE DERIVATIVES

Ucel, UI., Turan Yucel, N., Demir Ozkay, U., Can, OD.

Anadolu University, Department of Pharmacology, Eskisehir, Turkey

INTRODUCTION:

Based on the potential of benzimidazole and piperidine pharmacophores for central nervous system related activity (1,2), we have recently synthesized some novel benzimidazole-piperidine derivative compounds and reported their anti-nociceptive effects (3). In the present study, we aimed to examine the possible antidepressant-like actions of these benzimidazole-piperidine derivative compounds by using different in vivo techniques.

MATERIALS AND METHODS:

Adult BALB/c mice (30-35 g) were used for the tests. The potential of the benzimidazole-piperidine derivatives for antidepressant-like activity was evaluated by tail suspension test (TST) and modified forced swimming test (MFST). Moreover, the effects of the test compounds on spontaneous locomotor activity were explored by activity cage measurements. The experimental protocol of this study was approved by the Local Ethical Committee of Anadolu University (Turkey).

RESULTS:

In this study, data obtained from the TST and MFST indicated that reference drug fluoxetine (20 mg/kg) and the compounds 2c–2h significantly decreased the immobility time of mice compared to the control group. The decreased immobility time of the animals in both of the screening tests pointed out the antidepressant-like activity of these compounds. Moreover, in the MFST, the same compounds increased the swimming time of mice, without any alteration in the climbing duration. These data demonstrate that the serotonergic rather than the noradrenergic system plays a significant role in the antidepressant-like effects of the compounds 2c–2h. Unchanged horizontal and vertical locomotor activities of the animals revealed that the observed antidepressant-like effects were specific.

CONCLUSIONS:

In this study, antidepressant-like effects of the tested benzimidazole-piperidine derivatives have been demonstrated. Moreover, serotonin was suggested as the mechanism of action for the test compounds. Nevertheless, the exact mechanism of this pharmacological activity needs to be further clarified.

ACKNOWLEDGEMENTS:

Authors of the study thank to Assoc. Prof. Dr. Yusuf Özkay for his support in the synthesis studies.

REFERENCES:

1. Tantray et al., (2018). Bioorganic Chemistry, 77:393-401.
2. Zhou et al., (2016). Acta Pharmacologica Sinica, 37:1401-12.
3. Demir Ozkay et al., (2017). Turkish Journal of Chemistry, 41:672-84.

P-149: MODIFICATIONS OF SOLID DRUG DOSAGE FORMS IN PEDIATRIC PATIENTS

Ozdemir, N., Tecen Yucel, K., Aras, E., Celiker, A.

Hacettepe University, Department of Clinical Pharmacy, Ankara, Turkey

INTRODUCTION:

Pediatric patients are different from adults in terms of drug pharmacokinetics because of physiological development, age and weight. Additionally, most of the drug formulations are produced for adults and it is a troublesome process adjusting them for pediatric patients' convenience. It may be necessary to modify adult solid dosage forms by tablet splitting or capsule opening in order to give the exact dose in pediatric

patients. In this study, it was aimed to evaluate the modifiability of the solid dosage forms requiring splitting or opening in a childrens hospital.

MATERIALS AND METHODS:

This is a retrospective point prevalence study conducted in Hacettepe University Ihsan Doğramacı Children's Hospital inpatient services on 22nd January 2018. Patients using oral medication were included in the study. Clinical pharmacist reviewed patients' orders in terms of modifiability of solid dosage forms by using package inserts, Micromedex Solutions®, and the Handbook of Drug Administration via Enteral Feeding Tubes (Third Edition, 2015). Splittabilty for tablets and openability for capsules were evaluated. Descriptive statictics were used for results.

RESULTS:

One hundred and seventeen patients were using oral medication. The median number of the total drugs used by patients was 5 (min: 1, max: 30). Fifty nine percent of the patients were taking one or more medications in tablet form, 32.5% in capsule form. In 53.8% of the patients, it was necessary to split the tablets or open the capsules in order to give the calculated doses according to weight and age. Only 18 tablets (18.94%) could be splitted and 7 (7.36%) tablets should not be splitted in 95 tablets requiring modification. There was not any information about splitting for rest of the tablets in their package inserts. Twenty four capsule forms were required opening and 5 of them (20.83%) could be opened and 11 of them (45.83%) should not be opened. For 8 (33.33) capsule forms there was not any information about the openability.

CONCLUSIONS:

Administration of adult formulations to pediatric patients due to the unavailability of pediatric drug formulations may have negative consequences on the treatment process. It is necessary to pay attention to whether tablets and capsules are splittable or openable in order to avoid problems such as inadequate or increased efficacy.

REFERENCES:

1. Ivanovska V, Rademaker MAC, et al., (2014). Pediatric Drug Formulations: A Review of Challenges and Progress. Pediatrics; 134:361-372.

P-150: CLINICAL PHARMACIST INTERVENTIONS IN GERIATRIC OUTPATIENT CLINIC AND CLINICAL NUTRITION UNIT

[1] Firat, O., [1] Kelleci, B., [2] Balci, C., [2] Esme, M., [2] Aycicek Sengul G., [1] Ekincioglu, A., [2] Halil, M., [1] Demirkan, K.

[1]Hacettepe University, Faculty of Pharmacy, Department of Clinical Pharmacy, Ankara, Turkey

[2]Hacettepe University, Faculty of Medicine, Department of Internal Disease, Division of Geriatric Medicine, Ankara, Turkey

INTRODUCTION:

Clinical pharmacy services needed up most in geriatric medicine and clinical nutrition units due to common polypharmacy and complicated medication administration process. Clinical pharmacists are monitoring the patients in collaboration with physician to provide rational therapy including appropriate drug administration and to reduce hospital stay (1, 2). The aim of this study was to evaluate the medication treatment and to identify the related problems by the clinical pharmacist in routine monitoring of the patients in outpatient clinics and in hospital.

MATERIALS AND METHODS:

Patients over 65 years old or followed up by nutritional support team (NST) in the university hospital were included in this study. Related information was recorded from patients' hospital files, hospital database (Nucleus), and the physicians during rounds by two clinical pharmacists. Online databases such as "Micromedex Trusted Evidence And Solutions - Truven Health Analytics®" and Medscape Drug Interaction checker® and various books such as "Handbook of Drug. Administration via. Enteral Feeding Tubes. Third Edition." were used to identify the interventions.

RESULTS:

During the study, 150 patients who were eligible according to the inclusion criteria were evaluated between February 1st and March 31st, 2018. Interventions categorized according to the types of problems such as drug-drug interaction (n=4, 13.3%), drug-nutrient interaction (n=2, 6.6%), drug side effect (n=10, 33.3%), counseling to the clinicians (n=7, 23.3%), wrong drug administration (n=5, 16.7%), clinical nutrition complication (n=2, 6.6%). Total of 30 interventions were made during the study period. Of those, 23 (76.6%) of them belong to geriatric outpatient clinic and 7 (23.3%) of them belong to clinical nutrition unit. Only 2 (6.6%) of these interventions has been not accepted by clinicians.

CONCLUSION:

The interventions made by clinical pharmacists would be beneficial to improve treatment outcomes and also to reduce drug-related problems and complications while working as a team member in these units.

REFERENCES:

1. Hanlon JT, Lindblad CI,et al., (2004). The American journal of geriatric pharmacotherapy, 2(1):3-13.
2. Kaur S, Mitchell G, et al., (2009). Drugs & aging, 26(12):1013-1028.

P-151: DETERMINATION OF POTENTIAL DRUG-DRUG INTERACTIONS IN NEPHROLOGY CLINIC

Gun, ZU., Gok, S., Bahcecioglu, OF.

Inonu University, Department of Clinical Pharmacy, Malatya, Turkey

INTRODUCTION:

The main goals of drug treatment include increasing the quality of life of the patient and minimizing drug-related problems. Hospitalized patients need more attention regarding potential drug-drug interactions (pDDIs) due to complexity of their disease (1). Our study aimed to determine the prevalence and significancy of pDDIs in nephrology patients.

MATERIALS AND METHODS:

This was a prospective study to find out types and prevalence of pDDIs in the Department of Nephrology and to share relevant interactions with physicians. Charts were assessed for prevalence and severity of pDDIs using the Medscape drug reference database. Severity was classified as “contraindicated”, “serious/ use alternative”, “monitor closely” and “minor”; significancy was evaluated by clinical pharmacists.

RESULTS:

The evaluation of pDDIs were observed in 46 charts and 3 patients were excluded since they were not using any medications. Eightynine (20.22%) out of 440 interactions were evaluated as “not significant”, because of the expected beneficial effects or different administration routes. Ninetyeight (22.27%) of pDDIs do not require any intervention. Interactions which need monitoring intervention classified as “monitor electrolytes” 93 (21.13%) (potassium etc.), “monitor blood drug levels” 40 (9.09%) (cyclosporin etc.); “monitor blood pressure” 41 (9.31%), “monitor blood sugar” 17 (3.82%). Intervention for changing route of administration was 27 out of 440 (6.13%) and changing administration time was 16 (3.63%). Also, 4 (0.91%) of these interactions were solved by changing of drug like gabapentin to pregabalin. Most detected pDDI was monitor potassium (16,59%).

CONCLUSIONS:

According to a review of 21 studies, clinical pharmacist-led programmes increase medication knowledge, decrease hospitalization rates, and improve quality of life (2). A study in Australia has shown that pharmacists play a vital role in reducing drug-related problems and increasing treatment efficacy (3). It was a limiting factor that the patient count in our study was low. It is necessary to study more about the pharmaceutical care service and the results of the pharmacist’ role in a larger population.

REFERENCES:

1. Fasipe OJ, et al., (2017). Clinical Pharmacology: Advances and Applications, 9: 125–132
2. Stemer G, Lemmen Gruber R (2011). BMC Nephrology, 12-35
3. Ghimire S, et al., (2018). Int. J. Of Clinical Pharmacy, 40: 26-35

P-152: EVALUATION OF KNOWLEDGE AND ATTITUDES OF PATIENTS USING EYE DROPS / OINTMENTS

Kilicaslan, O., Sancar, M., Tezcan, S., Izzettin, FV.

Marmara University, Faculty of Pharmacy, Clinical Pharmacy Department, Kadıköy, Istanbul, Turkey

INTRODUCTION:

Administration of ocular medications should be done according to the principles of rational drug use. The aim of our study was to evaluate the level of knowledge and attitudes of patients using eye drops/ ointments.

Material and Methods: A total of 105 patients who were prescribed eye drops/ointments between 20 January and 1 March 2018 were included in the study. The study was conducted on a community pharmacy in Istanbul/Turkey Knowledge and attitudes of patients using eye drop / ointment were evaluated by a questionnaire consisted of a total of 20 questions. The results were considered to be significant at $p < 0.05$ in the 95% confidence interval.

RESULTS:

The mean age of the patients was 36.42 ± 1.23 (18-77) and 65.7% (n = 69) were female patients. Fifty six point two percent (n = 59) of the patients were graduated from university and 87.6% (n=92) of patients were prescribed two or more eye drops/ ointments. Sixty two point nine percent of the patients (n=66) reported that they had patient education about usage of eye drugs and 45.5% (n =30) of these patients were informed by the pharmacist. When the patients were asked if eye drops and eye ointment were prescribed together, which one of them should be applyed firstly, 73.3% (n =77) of the patients stated that they first applied eye drops. The patients with

university degree answered correctly this question statistically higher than the other patients ($p<0.05$). Forty percent of the patients (n =42) stated that they waited five minutes between eye drop and ointment application. Thirty five point two percent of patients reported that the ointment had to be kept for 28 days after opening and 27.6% (n =29) of the patients reported that eye drop bottles should be kept for 15 days after opening.

CONCLUSIONS:

In our study, application errors were observed with the usage of eye drugs. We believe that pharmacists will have a significant contribution in rational use of eye drugs by the patient education.

P-153: THE EFFECT OF ATOMOXETINE TREATMENT ON MECHANICAL- AND THERMAL-HYPERALGESIA DEVELOPING IN DIABETIC RATS

Barbaros, MB., Can, OD. Demir Ozkay, U.

Anadolu University, Faculty of Pharmacy, Department of Pharmacology, Eskişehir, Turkey

INTRODUCTION:

Peripheral neuropathy is one of the common complications of Diabetes mellitus. Enhanced sensitivity to touch; severe pains or cramps; sensation of burning or tingling, reduced ability to feel nociception or temperature alterations, loss of reflexes, loss of balance and coordination are among the chief symptoms of peripheral neuropathy (1). Strengthen of monoaminergic neurotransmission in the supraspinal pain pathways are known to induce analgesic effect against neuropathic pain. Based on this knowledge, we planned to investigate possible therapeutic effect of atomoxetine, a selective noradrenaline reuptake inhibitor, on mechanical- and thermal-stimuli induced hyperalgesia perception, developing in diabetic rats.

MATERIALS AND METHODS:

Male Sprague-Dawley rats were used for the experiments. A single 50 mg/kg dose of streptozotocin were intravenously injected to induce diabetes. Four weeks after the induction of diabetes, time required for development of hyperalgesia, daily atomoxetine administrations (50 mg/kg/day, po) was started. At the end of the two weeks treatment period, effect of atomoxetine on mechanical and thermal hyperalgesia was assessed using Randall-Selitto and Hargreave's tests, respectively (2). The experimental protocol of this study was approved by the Anadolu University Animal Experiments Local Ethics Committee.

RESULTS:

"Paw-withdrawal threshold" and "paw-withdrawal latency" values of diabetic rats, measured in Randall-Selitto and Hargreave's tests respectively, were significantly lower than that of the normoglycemic animals. However, treatment with atomoxetine for two weeks significantly increased both of these reduced values, indicating the notable anti-hyperalgesic efficacy of this drug.

CONCLUSIONS:

Obtained data revealed that atomoxetine has a potential for treatment of diabetes-induced hyperalgesia. However, further clinical studies are needed to confirm the results of this preclinical study.

ACKNOWLEDGEMENTS:

This work was financially supported by the Anadolu University Research Foundation (No. 1705S549).

REFERENCES:

1. Ucell Uİ, Can OD, Demir Ozkay U, Ozturk Y (2015). European Journal of Pharmacology, 756:92-106.
2. Boulton et al., (2005). Diabetes Care, 28:956-962.

P-154: ANTI-NOCICEPTIVE EFFECT OF SOME BENZOTHIAZOLE DERIVATIVES

Turan Yucel, N., Ucel, UI., Can, OD., Demir Ozkay, U.

Anadolu University, Faculty of Pharmacy, Department of Pharmacology, Eskisehir, Turkey

INTRODUCTION:

Our research group has recently reported the synthesis and antidepressant-like activities of some novel benzothiazole derivatives (3a–3h) (1). In the present study, based on the analgesic activity potential of antidepressants (2) as well as the central nervous system related pharmacological activity capacity of benzothiazole pharmacophore (3), we planned to investigate anti-nociceptive efficacy potential of these compounds.

MATERIALS AND METHODS:

Experiments were performed with adult BALB/c mice (30-35 g). Anti-nociceptive effect was evaluated by tail-clip, hot-plate and acetic acid-induced writhing tests. Probable effects of test compounds on motor coordination of mice were evaluated by the Rota-Rod test. The experimental protocol of this study was approved by the Local Ethics Committee on Animal Experimentation of Anadolu University, Turkey.

RESULTS:

In the tail-clip and hot-plate tests, reference drug morphine (10 mg/kg) and compounds 3f, 3g and 3h administrated at 40 mg/kg doses significantly increased the reaction time of animals against mechanical and thermal nociceptive stimulus, respectively. According to this data, it may be suggested that anti-nociceptive activities of these compounds are related to both supraspinal and spinal mechanisms. Moreover, in

acetic acid-induced writhing test, morphine and compound 3e significantly reduced the number of abdominal contractions and stretches induced by chemical noxious stimuli, indicated the peripherally mediated anti-nociceptive activity of this compound. In the Rota-rod tests, falling latencies of mice did not change upon the administration of test compounds, therefore observed anti-nociceptive effect seemed to be specific.

CONCLUSIONS:

Results obtained from the nociceptive tests indicated that compounds 3f, 3g and 3h show centrally mediated anti-nociceptive activities whereas anti-nociceptive effect of compound 3e was related to peripheral mechanisms. Nevertheless, the exact mechanisms of the observed anti-nociceptive action required to be clarified with further detailed investigations.

ACKNOWLEDGEMENTS:

Authors of the study thanks to Assoc. Prof. Dr. Yusuf Özkay for his supports in the synthesis studies.

REFERENCES:

1. Demir Özkay Ü et al., (2017). Molecules. 22:pii:E1490.
2. Sindrup et al., (2005). Basic & Clinical Pharmacology & Toxicology, 96:399-409.
3. Wang et al., (2014). Bioorganic & Medicinal Chemistry Letters, 24:1766-1770.

P-155: WOUND HEALING EFFECT OF VITEXIN FORMULATION

[1] Arslan, R., [1] Bektas Turkmen N., [2] Senel B., [3] Yenilmez E., [4] Ozatik O.,

[1] Anadolu University, Department of Pharmacology, Eskisehir, Turkey

[2] Anadolu University, Department of.Pharmaceutical Biotechnology, Eskisehir, Turkey

[3] Anadolu University, Department of.Pharmaceutical Technology, Eskisehir, Turkey

[4] Dumlupinar University, Department of Histology and Embryology, Kutahya, Turkey

INTRODUCTION:

Skin is a protective barrier for the human body against the environmental attacks such as infections, injury and incision. The wound is described as the deterioration of anatomical and functional integrity of the living tissue (1). Wound healing is one of the major medical issues. It is known that several natural products, like flavonoids, promote the process of wound healing (2). Vitexin is a known flavonoid found in many medicinal plants composition. It has antinociceptive, anti-oxidant, anti-inflammatory, anti-viral, cardioprotective, and antibacterial effects (3). In the present study, we aimed to investigate the in vivo and in vitro healing effect of vitexin loaded chitosan gel formulations.

MATERIALS AND METHODS:

The rats were anaesthetized and their dorsal hairs were removed by shaving. The circular wound (10-12mm) was created on the dorsal interscapular region of each animal by excising the skin with a scissors. Animals were divided into 4 groups: control (no treatment), positive control (madecassol® treatment), vehicle (chitosan), formulation treated group (chitosan+vitexin). The animals were anaesthetized and wound area was removed for histological analysis. Extracted parts were stained with H & E and Masson Trichrome and histopathologic changes in dermis and epidermis were investigated. The wound healing effect of the formulations were assessed by measuring the diameter of the wound by a digital caliper and photographs of wounds were taken at 0, 7th, 14th and 21st days of treatment. Chitosan-based gel formulation containing vitexin, madecassol and vehicle were applied every morning and evening (4).

RESULTS:

When compared to the control group, progressive healing were observed on wound in treated rats with vitexin formulation. According to our macroscopic results, it is determined that vitexin formulation was about as potent as positive control madecassol®. Histological examinations showed that, epidermal and dermal regeneration, granulation and angiogenesis was promoted by vitexin formulation. It was found that Vitexin formulation provide reepithelization and wound healing in shorter time.

CONCLUSIONS:

This study demonstrated that vitexin formulation possess an accelerating effect on wound healing. We think that vitexin loaded formulations will contribute to new therapeutic approaches and new drug development studies on wound healing.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Anadolu University BAP (BAP-1605S310)

REFERENCES:

1. Yenilmez E, et al., (2015). Pharmazie, 70(2):67-73.
2. Kumar B, et al., (2007). Ethnopharmacol, 1;114(2):103-13.
3. He M, Min JW, Kong WL, He XH, Li JX, Peng BW (2016). Fitoterapia, 115:74-85.
4. Nayak SB, et al., (2017). Advances in wound care, 6(12):401-406.

P-156: THE PERCEPTION OF COMMUNITY PHARMACIST TO ANTIDEPRESSANT MEDICATIONS DURING PATIENT COUNSELING IN NICOSIA, NORTHERN CYPRUS

[1] Khamis, S., [1] Abdi, MA.,[1,2] Basgut, B.

[1]Near East University, Faculty of Pharmacy, Department of Clinical Pharmacy, Nicosia, North Cyprus

[2]Near East University, Faculty of Pharmacy, Department of Pharmacology, Nicosia, North Cyprus

INTRODUCTION:

Antidepressants are group of drugs which need an appropriate consultation to be used rationally. Non-adherence to antidepressant medications is a common problem in the treatment of depression, and has been associated with adverse outcomes (1). Effective interactions between patients and health care practitioners as community pharmacists have been shown to be important in patients' acceptance of antidepressant (2). The study is aimed to evaluate the community pharmacists' counseling practices in response to antidepressant medication compliance.

MATERIALS AND METHODS:

In Nicosia, Northern Cyprus, 80 community pharmacists received two simulated patient visits at different times. The scenarios were concerning the use of antidepressant medications and adherence with therapy. These scenarios were developed by a research team based on literature (1). The first scenario was of a patient receiving a first-time antidepressant prescription and hesitant to begin treatment. The second scenario was of a patient perceiving lack of treatment efficacy for antidepressant after starting treatment for 2 weeks. The interactions were recorded and analyzed to evaluate the content of consultations in terms of information gathering, information provision including key educational messages, and treatment recommendations.

RESULTS:

Each pharmacist received 2 simulated patient visits, resulting in 160 encounters. Information gathering in both scenarios was 28.8%. In scenario 1, 18.3% of gathering questions were asked while in scenario 2, 39.3% were asked. In scenario 1 the question most frequently asked by pharmacists was about the information given by the general practitioner about antidepressants (61%). In scenario 2, the question "if the patient has sought medical help for depression or is taking an antidepressant" was asked by 81%. In scenario 1 no one asked if the patient has any other medication whereas in scenario 2 only one pharmacist asked. In terms of information provision, information items most frequently provided in scenario 1 were the technical information "how to use and the dosage" (99%), but no one provides information about serotonin reuptake inhibitors (SRI). In scenario 2 most information provided were the time frame to use antidepressant (90%) and precaution about use of St John's wort together with antidepressants (56%).

CONCLUSION:

This study shows poor information role practice of pharmacists in North Cyprus related to antidepressants use and their delivery of adherence message. The results highlight the need of the community pharmacists for further training in the area of antidepressant medications' consultation to enhance the care provided for psychiatric patients.

REFERENCES:

1. Chong WW, Aslani P, et al., (2013). Adherence to antidepressant medications: an
2. evaluation of community pharmacists' counseling practices, 813–825.
3. Chong WW, Aslani P, et al., (2014). Pharmacist–patient communication on use of antidepressants: A simulated patient study in community pharmacy 419–437.

P-157: IN VIVO ANTINOCICEPTIVE AND ANTIINFLAMMATORY EFFECTS OF FRAXINUS ANGUSTIFOLIA EXTRACTS

[1] Sevgi S., [2] Cavusoglu I., [1] Eroglu G., [3] Temiz B., [3] Tetik S., [4] Renda G., [1] Kaya Yasar Y.

[1]Karadeniz Technical University, Faculty of Pharmacy, Department of Pharmacology, Trabzon, Turkey

[2]Karadeniz Technical University, Faculty of Medicine, Department of Pharmacology, Trabzon, Turkey

[3]Karadeniz Technical University, Faculty of Pharmacy, Undergraduate Student, Trabzon, Turkey

4Karadeniz Technical University, Department of Pharmacognosy, Trabzon, Turkey

INTRODUCTION:

Fraxinus (F.) angustifolia is commonly used for inflammation and pain in folk medicine. We showed that the methanol extract (MEFA) of F. angustifolia Vahl barks has dose-dependent antinociceptive and antiinflammatory activity in mice (1). In this study, effects of the sub-extracts of MEFA were evaluated using hot-plate and formalin-induced edema test to further investigate the fractions of this plant responsible for the antinociceptive and anti inflammatory actions.

	15. minute	30. minute	45. minute	60. minute
Control (%5 DMSO-saline)	6.24±2.02	7.23±4.09	3.34±1.68	0.68±0.68
WAS	4.67±3.94	17.90±6.66	17.36±5.54	13.83±5.38
EAS	13.50±2.66	11.68±4.76	23.40±6.30	17.44±5.94
DMS	30.48±5.18*	22.94±5.27	30.70±6.58*	37.60±10.13**
Morphine	58.59±9.03#	54.10±10.67#	62.73±10.11#	55.26±9.46#

Table 1. MPE% values of vehicle, sub-extracts and morphine. The data were expressed as mean±SEM (n=6-8).

**P<0.05, **P<0.01, #P<0.001, significantly different from control.*

MATERIALS AND METHODS:

The barks of F. angustifolia Vahl were collected from Ortahisar, Trabzon; water (WAS), ethyl acetate (EAS) and dichloromethane (DMS) sub-extracts of MEFA were prepared. In the hot-plate test, vehicle, sub-extracts (100 mg/kg) or morphine (10 mg/kg) were administered intraperitoneally (i.p.) to male mice (Balb/c; 20-30 g); beginning time of paw licking and jumping behavior were measured before (baseline) and after the applications (latency) at 15 minutes intervals and the analgesic activity was calculated as the maximum possible effect (MPE%). In the formalin-induced edema test, 30 minutes before the epidermal injection of 1% formalin, vehicle, sub-extracts (100 mg/kg) or diclofenac (10 mg/kg) were administered i.p.mice; paw thickness (measured with a compass) and paw volume (measured with a plethysmometer) were recorded before and 30 minutes after formalin injection and the amount of edema was calculated as the difference between the two values. Statistical analysis was performed by using ANOVA/Tukey; P<0.05 is considered significant.

	Paw thickness (mm)	Paw volume (ml)
Control (saline)	0.99±0.03	0.07±0.007
Control (5%DMSO-saline)	0.74±0.05	0.04±0.003
WAS	0.45±0.03*	0.03±0.002*
EAS	0.51±0.03#	0.03±0.003
DMS	0.67±0.02	0.03±0.002
Diclofenac	0.68±0.03*	0.04±0.006*

Table 2. Paw volume and thickness values of vehicle, sub-extracts and diclofenac. The data were expressed as mean±SEM (n=8).

**P<0.05 significantly different from control (saline)*

#P<0.05 significantly different from control (5% DMSO-saline).

RESULTS:

DMS and morphine significantly increased MPE% values compared to control; whereas WAS and EAS did not alter MPE% values (Table 1). WAS, EAS and diclofenac significantly reduced the paw thickness; while WAS and diclofenac significantly decreased paw volume compared to control (Table 2).

CONCLUSIONS:

DMS and WAS sub-extracts of MEFA demonstrated potent antinociceptive and antiinflammatory activity, respectively, indicating that selective compounds in these fractions are responsible for the bioactivity of F. angustifolia. Investigation of the contents of the sub-extracts and the mechanism of action of these compounds in future studies will be essential for the development of potential new therapeutics.

REFERENCES:

1. Sevgi S., Cavusoglu I., Kaya-Yasar Y., Sezen FS., Duman M., Gumus Z., Aydın G. Anti-nociceptive and Anti-inflammatory Effects of Methanolic Extract of Fraxinus Angustifolia, 3rd International Convention of Pharmaceuticals and Pharmacies, 26-29 April 2017, Istanbul, 1019-1019.

P-158: ASSESSMENT OF BREAST CANCER THERAPY IN A HOSPITAL: A RETROSPECTIVE STUDY

[1] Durmazpinar, S., [2] Taner, N., [1] Macit, C.

[1]Istanbul Medipol University, School of Pharmacy, Department of Pharmacology, Istanbul, Turkey

[2]Istanbul Medipol University, School of Pharmacy, Department of Clinical Pharmacy, Istanbul, Turkey

INTRODUCTION:

Breast cancer is the most common cancer type in women in both developed and developing countries. It is one of the major cause of cancer deaths in women.1 It is estimated that the incidence of female breast cancer worldwide will reach approximately to 3.2 million annually in 2050.2 The objective of this study was to examine the assessment of breast cancer therapy in a hospital.

MATERIALS AND METHODS:

This study is a retrospective study that conducted in women over the age of 18 years. It was performed in a hospital between the years of 2017 and 2018. Patient files were reviewed after having the approval of the committee of ethics. The rate of cancer was assessed in terms of the age of the patients. The incidence of breast cancer, calcium supplementation, medications used and metastasis were studied.The data were analyzed with SPSS V21 statistic program.

RESULTS:

The results of the study showed that the age range of the 40% of the patients were between 31 and 45 years and 43% of the patients were between 45 and 60 years. 70% of the patients had calcium supplementation. There is no significance between the right and left breast which has cancer($p<0.05$). 80% of patients had combined drug treatment.

CONCLUSION:

Breast cancer is common among women between the ages of 30-60. Additionally, most of the patients received combination therapy with calcium supplementation.

REFERENCES:

1. Rivera Franco MM, Leon-Rodriguez E (2018). Breast Cancer (Auckl). doi:10.1177/1178223417752677.
2. Tao Z, Shi A, Lu C, Song T, Zhang Z, Zhao J (2015). Cell Biochem Biophys, 72:333-338.

P-159: PRESENCE OF GXSXGY MOTIF ON N-TYPE VOLTAGE-DEPENDENT CALCIUM CHANNELS AND ANDROCTONUS CRASSICAUDA SCORPION TOXINS.

[1] Aydin, S., [2] Cakmak, A.

[1] Anadolu University, Faculty of Pharmacy, Department of Pharmacology, Eskisehir, Turkey

[2] Bozok University, Faculty of Medicine, Department of Pharmacology, Yozgat, Turkey

INTRODUCTION:

It is well known that among various actions, animal and scorpion envenomation results with severe painful conditions (1). On the other hand, analgesic actions of some animal toxins and the role of N-type calcium channels on these analgesic actions have been reported (2). In silico investigations of the structures of proteins and motifs residing on proteins, ion channels and receptors have been reported to have many important roles on their function. One of the motifs shown to be crucial on protein-protein interactions is GG4 motifs (3, 4). The aim of this study was to investigate the presence of GG4 motifs on Androctonus crassicauda toxins and calcium channels that are reported to play role on pain sensations.

MATERIALS AND METHODS:

The protein sequences belonging to voltage-dependent N-type calcium channel of human (CAC1B_HUMAN) and 24 toxins of Androctonus crassicauda scorpion were downloaded from uniprot database (www.uniprot.org). Protein sequences were extracted using Slackware GNU/Linux operating system. R/Bioconductor packages, Protr and Bio3d and ClustalW were used for alignment of proteins, statistical evaluation and plotting. Swiss-model, Swiss Pdb-viewer were used for 3D modelling and viewing.

RESULTS:

The results of our investigations showed the presence of GG4 motifs on voltage-dependent N-type calcium channel of human and only on 4 types toxins (SCX6, TX23, TX31 and TX32). There were 19 GG4 motifs on the calcium channel but there was only one GXSXGY motif having similarity with Androctonus crassicauda toxins. Alignment of these toxins and N-type calcium channel using ClustalW programme showed similar and shared GG4 motif with a tyrosine amino acid (GXSXGY motif).

CONCLUSIONS:

The presence of GXSXGY motif on Androctonus crassicauda toxins (TX23, TX31, TX32 and SCX6) and on voltage-dependent N-type calcium channel raised the question whether these toxins exert any action on N-type calcium channels resulting in unexpected analgesic effect. Further studies are required on these purified toxins.

REFERENCES:

1. Altinkkurt O, Altan M (1980). J. Fac. Pharmacy Ankara, 10: 41-60.
2. Adams DJ, Berecki G (2013). Biochim Biophys Acta, 1828:1619-1628.
3. Mueller BK, Subramaniam S, Senes A (2014). Proc Natl Acad Sci U S A. 111, E888-E895.
4. Teese MG, Langosch D (2015). Biochemistry, 54:5125-5135.

P-160: BEXAROTENE, A RXRA AGONIST, PREVENTS LIPOPOLYSACCHARIDE-INDUCED INFLAMMATORY HYPERALGESIA IN MICE

Kucukkavruk, SP., Temiz Resitoglu, M., Guden, DS., Sari, AN., Sahan Firat, S., Tunctan, B.

Mersin University, Department of Pharmacology, Mersin, Turkey

INTRODUCTION:

Inflammation leads to hyperalgesia which means decreased pain threshold or increased pain sensitivity. A selective retinoid X receptor α agonist, bexarotene (BEX), has been approved for the treatment of patients with cutaneous T-cell lymphoma. If used at appropriated doses, BEX is also reported to be beneficial in treating neurodegenerative diseases associated with systemic inflammation such as Parkinson's disease, Alzheimer's disease, and schizophrenia. The aim of this study was to determine the effective dose of BEX in lipopolysaccharide (LPS)-induced inflammatory hyperalgesia model in mice.

MATERIALS AND METHODS:

Male Balb/c mice were divided into 8 groups: (1) Saline, (2) LPS, (3) dimethyl sulfoxide (DMSO), (4) LPS+BEX (0.1 mg/kg), (5) LPS+BEX (1 mg/kg), (6) LPS+BEX (3 mg/kg), (7) saline+BEX (10mg/kg), and (8) LPS+BEX (10mg/kg). DMSO or BEX (4 ml/kg; s.c.) were administrated simultaneously with saline (10 ml/kg, i.p.) or LPS (10 mg/kg, i.p.). Reaction time to thermal stimuli within 1 min evaluated in mice received saline, LPS, DMSO, or BEX after 6 h.

RESULTS:

LPS caused a significant decrease in hot plate latency 6h after injection when compared to saline treated group ($P<0.05$). Only at 10 mg/kg dose BEX prevented the LPS-induced hyperalgesia 6 h after drug injection ($P<0.05$). The other doses of BEX were not effective to prevent the LPS-induced hyperalgesia ($P>0.05$). BEX at 10 mg/kg dose or DMSO had no effect on the hot plate latency in saline-treated mice ($P>0.05$).

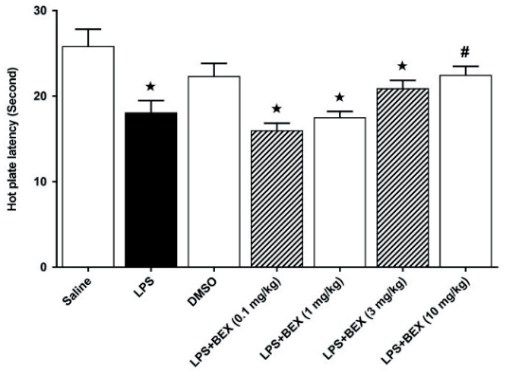


*Fig.1. * P<0.05 vs. saline-treated group. # P<0.05 vs. LPS-treated group.*

CONCLUSIONS:

These results demonstrate that BEX prevents inflammatory hyperalgesia induced by systemic LPS administration.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-217S235) and Mersin University (2018-1-TP3-2814)]

P-161: COMPARATIVE ASSESSMENT OF AWARENESS AND ATTITUDES OF COMMUNITY PHARMACISTS IN NORTHWEST NIGERIA AND MUĞLA, TURKEY TOWARDS CHRONOTHERAPY

Chukwunyere, U., Bilge, S., Abacioglu, N.

[1]Near East University, Faculty of Pharmacy, Department of Pharmacology, Lefkosa/Mersin[1]0, Turkey

INTRODUCTION:

Chronotherapy refers to the use of endogenous biologic rhythms to optimize therapy. The importance of time of administration of medication cannot be overemphasized in clinical practice. Therefore, this study was designed to assess and compare the awareness and attitudes toward chronotherapy among community pharmacists practicing in Northwest Nigeria and Muğla, Turkey.

MATERIALS AND METHODS:

A three month cross sectional study of 125 and 152 community pharmacists practicing in Northwest Nigeria and Muğla respectively, was conducted in 2017 and data was collected using a modified questionnaire based on current literature (1). The questionnaire which comprised of twenty seven items, explored the participants' demography, knowledge, attitude and willingness to apply the principles of chronotherapy in future practice. Descriptive statistics were used to report the demographics while *Mann–Whitney U test was used to compare the mean total awareness and attitude scores.*

RESULTS:

Data analysis showed that community pharmacists in Muğla have a statistically significant higher mean total awareness score 9.46 ± 1.63 ($P < 0.05$) and a lower mean total attitude score 44.26 ± 6.25 when compared with community pharmacists in Northwest Nigeria with lower mean toal awareness score 8.49 ± 1.38 and a statistically significant higher mean total attitude score 46.19 ± 5.92 ($P < 0.05$). Results also showed that years of practice influenced the awareness scores in both regions.

CONCLUSIONS:

The community pharmacists in Muğla have more knowledge about chronotherapy; however, their attitudes toward applying their knowledge in future practice was lower when compared with community pharmacists in Northwest Nigeria. These findings reaffirm the need for educational programs targeted at sensitizing pharmacists on the importance of chronotherapy in pharmacy practice.

ACKNOWLEDGMENT

We acknowledge all community Pharmacists that participated in this study.

REFERENCES:

1. Kaur G, Phillips C, Wong K, Saini B (2016). Sleep Biol. Rhythms, 14:329–338

P-162: THE EFFECT OF TOFISOPAM TREATMENT ON GLIAL PLASTICITY IN RAT HIPPOCAMPI

[1] Ucel, UI., [1] Demir Ozkay, U., [2] Ulupinar E, [1] Can OD.

1. Anadolu University, Department of Pharmacology, Eskisehir, Turkey
2. Eskisehir Osmangazi University, Department of Anatomy, Eskisehir, Turkey

INTRODUCTION:

We have recently reported beneficial effects of tofisopam, a 2,3-benzodiazepine derivative anxiolytic drug, on scopolamine-induced amnesia model (1). Furthermore, we have demonstrated that tofisopam treatment increases proliferation of the neurons in the sub-granular zone of dentate gyrus, suggesting a beneficial potential for tofisopam on hippocampal neurogenesis (2). In the present study, based on the functional capacities of astrocytes on learning and memory processing (3), we aimed to investigate probable effect of this drug on glial plasticity in the hippocampus.

MATERIALS AND METHODS:

Rats were treated with tofisopam (50 mg/kg/day p.o.) for one week. Amnesia was induced by scopolamine administration (0.5 mg/kg i.p). After anesthesia, rats were transcardially perfused with

PBS and PBS - 4% paraformaldehyde solution. Brain hemispheres including the dorsal hippocampus were embedded in paraffin, sectioned at 3 µm thickness and stained immunohistochemically for further quantitative analysis. The boundaries of the hippocampal subregions were defined according to the stereotaxic rat brain atlas. Photomicrographs were taken under light microscope by integrated camera. GFAP immunoreactive area per unit area was calculated by using Image J analysis program. The experimental protocol of this study was approved by the Anadolu University Animal Experiments Local Ethics Committee.

RESULTS:

Obtained data indicated that, in amnesic rats, GFAP densities per unit area in the hippocampal DG, CA1 and CA3 subregions were significantly reduced with respect to the control group. However, tofisopam treatment increased the GFAP immunoreactivity in amnesic rats compared to untreated amnesic animals in all regions of hippocampal formation.

CONCLUSIONS:

Our findings demonstrate that tofisopam treatment restored the impaired astrocyte activation of amnesic rats. This effect of tofisopam on glial plasticity might be contributed to its anti-amnesic efficacy. However, further detailed studies are needed to clarify exact mechanisms underlying the nootropic action of tofisopam.

REFERENCES:

1. Ucel UI et al., (2017). IVEK 3rd International Convention of Pharmaceuticals and Pharmacies P(0778), 1028.
2. Ucel UI et al., (2017). 2nd International Gazi Pharma Symposium Series P(76), 145
3. Kurosinski P, Götz J (2002) Archives of Neurology 59 (10):1524-1528.

P-163: ANXIOLYTIC-LIKE EFFECT OF METHANOLIC EXTRACT PREPARED FROM HYPERICUM HIRCINUM L. SUBSP. MAJUS (AITON) N. ROBSON HERBA

[1] Saltan, N., [2] Ucel UI., 1 Kose YB., [2] Can OD.

[1] Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Eskisehir, Turkey

[2] Anadolu University, Faculty of Pharmacy, Department of Pharmacology, Eskisehir, Turkey

INTRODUCTION:

Several Hypericum L. (Hypericaceae) species, Hypericum perforatum L. in particular, have been reported to induce various pharmacological activities related to the central nervous system such as antidepressant, anxiolytic, analgesic and sedative effects (1). On the other hand, psychopharmacological effects of H. hircinum L. subsp. majus (Aiton) N. Robson, another well-known medicinal plant belonging to this family, have not been investigated in detail, so far. Therefore, in the present study, we aimed to examine anxiolytic potential of H. hircinum extract by using two different validated in vivo methods.

MATERIALS AND METHODS:

Male CD1 mice (30-35 g) were used for the experiments. Anxiolytic potential of the extract was assessed by using hole-board and plus maze tests, as described previously (2). In addition, probable effect of the extract on motor activity of animals was tested by Rota-rod tests. The experimental protocol of this study was approved by the Anadolu University Animal Experiments Local Ethics Committee.

RESULTS:

In the hole-board tests, methanolic extract of H. hircinum (2.5 and 5 mg/kg, i.p) increased the total number of head-dipping behavior together with the total number of holes explored. Additionally, in the plus-maze tests percentage of open entries as well as the percentage of time spent in the open arms increased by both of the administrated doses. Besides, in the Rota-rod tests, extract administrations did not change the falling latencies of animals.

CONCLUSIONS:

Acquired results indicated that H. hircinum has a significant anxiolytic-like activity, similar to some other species in the Hypericum genus. However, further clinical studies are needed to validate therapeutic potential of H. hircinum extract as an anxiolytic drug candidate.

REFERENCES:

1. Marrelli et al., (2016). Mini Reviews in Medicinal Chemistry,16:710-720.
2. Can ÖD et al., (2013). European Journal of Pharmacology, 699:250-257.

P-164: ANXIOLYTIC-LIKE ACTIVITIES OF SOME 1,3,4-THIADIAZOLE DERIVATIVES

[1] Can, OD., [1] Demir Ozkay, U., [2] Altintop, MD., [2] Kaplancikli, ZA.

[1] Anadolu University, Department of Pharmacology, Eskisehir, Turkey

[2] Anadolu University, Department of Pharmaceutical Chemistry, Eskisehir, Turkey

INTRODUCTION:

Thiadiazole is a five membered ring system carrying two nitrogen and one sulfur atom as chemical structure. Thiadiazoles may exist in four isomeric forms as 1,2,3-thiadiazole, 1,2,5-thiadiazole, 1,2,4-thiadiazole and 1,3,4-thiadiazole. Among them, especially

1,3,4-thiadiazoles are of great interest in the drug development studies as important pharmacophore groups (1). For example, antidepressant, anxiolytic, analgesic and anticonvulsant activities have been reported for various 1,3,4-thiadiazole derivatives so far (2,3). Based on the aforementioned central nervous system related efficacy potential of thiadiazole derivatives (4), in the present study we aimed to investigate possible anxiolytic-like activities of some 1,3,4-thiadiazole derivatives.

MATERIALS AND METHODS:

Balb/c mice, weighing 30-35 g, were used for the tests. Anxiolytic-like activity potential of the thiadiazole derivatives (100 mg/kg, i.p) was assessed using hole-board and plus-maze tests. Besides, motor coordination of the animals was evaluated using Rota-rod tests. The experimental protocol of this study was approved by the Anadolu University Animal Experiments Local Ethics Committee.

RESULTS:

In the plus-maze tests, reference drug diazepam, N-(benzothiazol-2-yl)-2-[(5-((4-nitrophenyl)amino)-1,3,4-thiadiazol-2-yl)thio]acetamide (3g) and N-(6-nitrobenzothiazol-2-yl)-2-[(5-((4-nitrophenyl)amino)-1,3,4-thiadiazol-2-yl)thio]acetamide (3h) increased the percentage of open arms entries as well as the percentage of time spent in these arms. Besides, in the hole-board tests, reference drug diazepam and the same compounds increased the total number of the head-dipping behavior as well as the total number of holes explored. Moreover, these two compounds did not alter the falling latencies of animals examined in the Rota-rod tests.

CONCLUSIONS:

Obtained data indicated that compounds 3g and 3h possess significant anxiolytic-like activities without any non-specific effect on motor coordination of animals. Moreover, the results of this study supported the previous papers reporting the efficacy potential of 1,3,4-thiadiazole derivatives on the central nervous system.

REFERENCES:

1. Siddiqui N et al., (2009). Journal of Chemical and Pharmaceutical Research, 1:19-30.
2. Pattanayak P, Sharma R, Sahoo PK (2009). Medicinal Chemistry Research, 18:351-361.
3. Sharma R, Misra GP, Sainy J, Chaturvedi SC (2011). Medicinal Chemistry Research, 20:245-253.
4. Altıntop MD, Can ÖD, Demir Özkay Ü, Kaplancıklı ZA (2016). Molecules, 21(8):1004.

P-165: ANTIDEPRESSANT-LIKE EFFECT OF NOVEL BENZAZOLE DERIVATIVES

[1] Tokgoz, G., [1] Demir Ozkay, U., [2] Osmaniye, D.,[1] Can, OD.

[1] Anadolu University, Department of Pharmacology, Eskisehir, Turkey

[2] Anadolu University, Department of Pharmaceutical Chemistry, Eskisehir, Turkey

INTRODUCTION:

The benzazole type compounds including benzimidazole and benzothiazole rings have been reported to exhibit central nervous system (CNS) related effects such as antidepressant, anticonvulsant and analgesic activities (1-3). In the present study, based on the CNS-related activity potential of benzimidazole and benzothiazole scaffolds, we synthesized some novel compounds carrying these ring systems and investigated their potential antidepressant-like activities.

MATERIALS AND METHODS:

Target compounds (4a-4h) were obtained by the reaction of corresponding 2-(benzazol-2-ylthio) acetohydrazide and appropriate 4-substituted benzaldehyde. Pharmacological studies were carried out with adult BALB/c mice (30-35 g). Antidepressant-like activities of the test compounds (50 mg/kg) were evaluated using the tail suspension (TST) and the modified forced swimming tests (MFST). Besides, locomotor activity was assessed by activity cage measurements. The experimental protocol of this study was approved by the Local Ethics Committee on Animal Experimentation of Anadolu University, Turkey.

RESULTS:

Reference drug fluoxetine and the test compounds 4a, 4b, 4e and 4f significantly reduced the immobility duration of mice in both of the TST and MFST, pointing out the antidepressant-like effects of these compounds. Moreover, the same compounds augmented the swimming time of animals in MFST without any change in the climbing duration indicated that the observed antidepressant-like effects may probably be related to serotonergic rather than noradrenergic mechanisms in the CNS. Antidepressant-like effects of compounds 4a, 4b, 4e and 4f seemed to be specific since total number of horizontal or vertical locomotor activities of the mice was not changed upon the administration of these compounds.

CONCLUSIONS:

Antidepressant-like activities of compounds 4a, 4b, 4e and 4f seem to be related to the serotonergic system rather than the noradrenergic system. However, this consideration needs to be confirmed with further detailed studies.

REFERENCES:

1. Keri et al., (2015). European Journal of Medicinal Chemistry, 89:207-251.
2. Khan et al., (2016). Bioorganic & Medicinal Chemistry Letters, 26:4020-4024.
3. Barot et al., (2013). Mini-Reviews in Medicinal Chemistry, 13:1421-1447.

P-166: CENTRALLY MEDIATED ANTINOCICEPTIVE ACTIVITIES OF SOME PIPERAZINE DERIVATIVE COMPOUNDS

Ucel, Uİ., Kandemir, U., Ozkay Demir, U., Can, OD.

Anadolu University, Department of Pharmacology, Eskişehir, Turkey

INTRODUCTION:

Piperazine is a six-membered ring system containing two nitrogen atoms at 1th and 4th positions. Derivatives of the piperazine scaffold have been reported to possess various central nervous system (CNS) related pharmacological effects such as antidepressant, anxiolytic, antipsychotic, anticonvulsant, anti-Alzheimer and analgesic actions (1). Based on the activity potential of piperazine derivative compounds on CNS, in this study, we planned to synthesize some new compounds carrying piperazine pharmacophore in their structure and investigate their anti-nociceptive activity by some in vivo methods.

MATERIALS AND METHODS:

Wistar rats, weighing 250-350 g, were used for the experiments. Anti-nociceptive activity potential of the piperazine derivatives (10 mg/kg, i.p) was tested using hot-plate and Randall-Selitto tests, two well-known methods using to evaluate centrally mediated pain perception (2). Moreover, motor activity of the animals were assessed using a Rota-rod device. The experimental protocol of this study was approved by the Anadolu University Animal Experiments Local Ethics Committee.

RESULTS:

All of the tested compounds (2a-2h) increased the percentages of maximum possible effect as well as enhanced the paw withdrawal threshold values of animals assessed in the hot-plate and Randall-Selitto tests, respectively. Furthermore, in the Rota-rod tests, none of the test compounds changed the motor coordination of animals.

CONCLUSIONS:

Results of the present study showed that our new piperazine derivative compounds 2a, 2b, 2c, 2d, 2e, 2f, 2g and 2h have significant antinociceptive activities on central pathways carrying mechanical and thermal nociceptive stimuli. Besides, exhibited antinociceptive effects are specific, since the obtained data does not influenced by any possible impairments in the motor activity of rats.

ACKNOWLEDGEMENTS:

Authors of the study thanks to Assoc. Prof. Dr. Yusuf Özkay for his supports in the synthesis studies.

REFERENCES:

1. Shaquiquzzaman et al., (2015). European Journal of Medicinal Chemistry, 102:487-529.
2. Demir Özkay et al., (2017). Turkish Journal of Chemistry, 41:672-684.

P-167: DEONTOLOGICAL VIOLATIONS IN TURKEY'S COMMUNITY PHARMACIES

Kiran, B., Karaca, EG.

Ege University, Faculty of Pharmacy, Department of Pharmacy Management, Izmir, Turkey

INTRODUCTION:

Deontological violations are important in terms of reputation of public health, pharmacy profession, protection of public finance (1). The study aim is to determine types and prevalence of deontological violations reflected in records of High Honor Court (HHC) in Turkish Pharmacists' Association(TPA), to develop proposals on corrective and preventive occupational policies.

MATERIALS AND METHODS:

Cross-sectional. Violation types in disciplinary files in TPA Period-40 Working Report between 10.12.2015-30.09.2017 of HHC in TPA and submitted from 54 Regional Pharmacists Chamber in Turkey were classified according to classification method of deontological violations in 3-groups, and results were evaluated by frequency and percentage distributions (2).

RESULTS:

In the study, 32 deontological violation types and 112 criminal cases were detected. These violations were classified in 3-groups according to classification method used in the first and only study on deontological violations committed in Turkey's community pharmacies (1,2). Accordingly, it was found that "competition-based deontological violations" are in the first rank with 51 cases (45.6%), "TPA, Drug-Pharmacy Legislation violations" in the second with 50 cases (44.6%) and "Social Security Institution (SSI) protocol provisions violations" in the last rank with 11 cases (9.8%), and in all types of violation, "collusion" is in the first rank (30.4%).

CONCLUSIONS:

When compared Turkey's the first study based on 25-year records with 2015-2017 Report of HHC Period-40; it was seen that "competition-based deontological violations" in the first rank with 53% decreased to 46%,

"TPA, Drug-Pharmacy Legislation violations" with 24.6% increased to 44.6% and "SSI violations" with 22.4% decreased to 9.8%, but the frequency of case types didn't change (2). The most common violation types; "prescription collection and transfer"(17%), "non-compliance to watch and working hours" (10.7%) among "competition-based deontological violations", and "not delivering medication to patients and invoicing drugs to the institution" (3.6%) among SSI violations. In TPA, Drug-Pharmacy Legislation Violations; it is thought-provoking that "collusion" violation in the past (76.3%) is still the most common violation (68%) and being in the first rank increasing its share from (18.6%) to (30.4%) in all violations despite increasing punishments (1,2). Persistence of violation despite punitive sanctions aggravated by recent regulations suggests that it is not possible to solve only by punitive sanctions, and it must be get to the bottom of the problem.

REFERENCES:

1. Kiran B, Mandiracioglu A (2013).Türkiye Klinikleri j Med Sci., 33(3).635-647.
2. TEB. 40.Dönem Merkez Heyeti Calısma Raporu (2017). Fersa Matbaacılık Ankara, pp 409-418.

P-168: A VIEW ON PATIENTS' VIEW TO PHARMACIST-PATIENT COMMUNICATION FROM COMMUNITY PHARMACIES

Kiran, B., Karaca, EG., Hizal, OG.

Ege University, Faculty of Pharmacy, Department of Pharmacy Management, Izmir, Turkey

INTRODUCTION:

Today, change in pharmacy worldwide is based on "patient-centered care" paradigm. In this change, "communication" is one of the most important arguments (1). This study is planned to determine communication level between pharmacists and patients receiving counseling from community pharmacies and the effective factors upon it, identify patients' expectations from community pharmacies and pharmacists.

MATERIALS AND METHODS:

Cross-sectional. 20-question survey in two parts developed by researchers was used as data collection tool. The survey was applied by face-to-face interview technique to 330-persons over 18-years who served from Ege University, Medical Faculty Hospital and went to a community pharmacist between 19.01.2018-28.02.2018. Obtained data in 95% confidence interval was evaluated by frequency, percentage distribution, Chi-square, Mann-Whitney U, Kruskal-Wallis and post-hoc tests using SPSS-16 package program.

RESULTS:

330 people participated to the survey (54.2% female - 45.8% male). 50.9% of patients are college or faculty graduates and 80.9% stated that they always take their medicines from the same pharmacy. Relationship between educational background and taking medication from the same pharmacy was found statistically significant (Fisher's exact test p=0.033). 86.4% of patients said that they were asked and trusted for information from the pharmacist, 90% that they were answered clearly, 81.2% stated that all information about medicines and treatment were explained clearly, 75.5% indicated that they can easily ask again pharmacist the points they do not understand. It was determined that 70.6% expressed that they had enough time and 60.3% stated that they wanted to ask questions to the pharmacist instead of a foreman or a technician. In another study, 71% of patients stated that pharmacists did not give comprehensive medicine counseling, 49% expressed that pharmacist did not encourage to ask questions, 53.2% indicated that they do not trust pharmacists' knowledge (2).

CONCLUSIONS:

In this study, it was found that when educational level decreases, pharmacy dependency and confidence level to pharmacist increase, more than 3/4 participants are satisfied with counseling services. Concordantly, it is thought that inclusion of "Communication in Pharmacy" course to the pharmacy curriculum and post-graduation trainings can improve the counseling services' quality provided by community pharmacists.

REFERENCES:

1. McDonough RP, Bennett MS (2006). Am J Pharm Educ, 70(3):1-12.
2. Akshar SA et al., (2014). IOSR J Pharm, 4(11):8-14.

P-169: STRATEGIC COOPERATION IN THE TURKISH PHARMACEUTICAL INDUSTRY

Aydin Guldur, E., Ozcelikay, G.

Ankara University, Faculty of Pharmacy, Department of Pharmacy Management, Ankara, Turkey

INTRODUCTION:

Since companies operate on international markets, they need to develop new products and create new technologies to keep pace with global competition (1). To provide a sustainable competitive advantage, the relationship of businesses to strategic partnerships, mergers or acquisitions with other businesses is increasingly important and this situation is seen as a strategic necessity (2). The aim of this study is to examine the current situation and future outlook of strategic partnerships and acquisitions in Turkey between the years 2007-2017 in the pharmaceutical industry.

MATERIALS AND METHODS:

In this study, mergers and acquisitions data for pharmaceutical companies are obtained from reports prepared by PricewaterhouseCoopers (PwC), Ernst & Young and Deloitte.

RESULTS:

In 2009, there were 563 mergers or acquisitions worldwide with a total value of $ 161.2 billion.The effects of the global crisis were also seen in the pharmaceutical sector, and in 2010 mergers and acquisitions amounted to 548 contracts worth $ 51.5 billion, down by 68% in value. In 2013, Turkey was ranked 18th in the world pharmaceutical industry. Turkey's pharmaceutical market is estimated to take place 16th in the world in 2018 (3).

In Turkey's pharmaceutical industry, acquisitions took place rather than mergers between the years 2007-2017. It seemed that the general tendency was to purchase the near-total share of the company. According to the deal values announced to the market, the highest sales volume in terms of value was realized in 2007 and 2012.

CONCLUSIONS:

The advantages of mergers and acquisitions are: to benefit from advantages such as sales / marketing, finance, production capacity and market share, to catch synergy in the research portfolio, to reduce the need for excess and to focus on therapeutic categories.

Turkey is attracting the attention of companies operating on a global scale with a growing elderly population, increasing average life expectancy and drug consumption per person (4).

REFERENCES

3. Celik O (1999). Ankara Universitesi SBF Dergisi, 54(1):24-40.
4. Kahraman G, Ugurluoglu O (2016). Journal of Management and Economic Research, 14(4):198-221.
5. Bilim Sanayi ve Teknoloji Bakanlığı Türkiye İlaç Sektörü Strateji Belgesi ve Eylem Plani 2015-2018, (2015). p.16.
6. Unal M (2017). Türkiye İlac Sektöründe Verimlilik ve Rekabetcilik, Kalkınma Arastirmalari Merkezi, Yayin No: 29

P-170: A STUDY ON PHARMACY SOFTWARE PRODUCTS IN TURKEY

[1] Bulmus, G., [2] Ozcelikay, G.

[1] Turkish Pharmacists' Association, Ankara, Turkey

[2] Ankara University, Faculty of Pharmacy, Department of Pharmacy Management, Ankara, Turkey

INTRODUCTION:

In this project, a study on pharmacy software products has been deployed and some brief information is given under some specific topics. Additionally, a survey was conducted by some specific areas and pharmacists' opinions are noted in order to create a better-developed pharmacy program. Facts like the increase in number of drugs sold in pharmacies, the necessity of putting every sale into accounting process immediately, diversification of personal and corporate sales, supplying drugs from different chains of distribution, drug stock control etc. made it mandatory to create and develop supporting programs in pharmacies.

MATERIALS AND METHODS:

Survey forms about software products establish the base of this research method. For the survey, community pharmacy managing directors operating at 10 specific regions located in central Ankara were asked 19 questions face-to-face. As of 2017 working year, there are 2033 active community pharmacies at 10 specific regions located in central Ankara. The sample size is found to be n=323 and 318 of these surveys are put into perspective.

RESULTS:

It's found that 77.1% of the pharmacists think information transfer is much easier and faster with the program. 51,1% of the pharmacists believe that they can equip their patient without any electronic information sources whereas 29% of the pharmacists seem to have no solid opinion about the subject. 79.6% of them think automation programs are user-friendly. 59.1% of the pharmacists put their priority on stock control feature while choosing a program. 72.7% of the pharmacists believe they know how many products they have on their shelves and 74.6% believe they keep track of the products' expiry dates.

CONCLUSIONS:

Pharmacists choose among programs depending on the location of their pharmacies. They prefer one program over the other on financial reasons, not administrative ones. The usage and properties of software products for pharmacist is considerably high. With the advanced technology, pharmacists should also stay up to date and they should follow the developments on their field.

REFERENCES:

1. Altintas N (2001). TEB Meslekiçi Egitim Dergisi, 1:61-64.
2. Tig EO, Dulger GA, Hidiroglu S. Toklu HZ (2012). Marmara Pharmaceutical Journal, 16:29-35.
3. Sumbuloglu K, Sumbuloglu V (1995). In: Biyoistatistik. Ankara, Ozdemir Yayıncilik.

P-171: AN ANALYSIS OF WORKFLOW AND WORK POWER IN COMMUNITY PHARMACIES IN ANKARA

[1] Zanbak, M., [2] Uzun, MB, [2] Ozcelikay, G.

[1] Turkish Pharmacists Association, Ankara, Turkey

[2] Ankara University, Faculty of Pharmacy, Department of Pharmacy Management, Ankara, Turkey

INTRODUCTION:

In addition to patient consultancy and dispensing duties, pharmacists in pharmacies also carry out administrative tasks such as inventory control, expiration date control, ordering medicines, employee training, and drug disposal. It is important in terms of pharmacy management to carry out all these works in a healthy way (1). In order to operate a community pharmacy in a healthy manner, it is necessary to determine workload and workflow of the employees. Increasing the quality of community pharmacy services will be possible through workload and workflow analyzes (2). This study is aimed to reveal the workflow in community pharmacies and evaluate the workflow in terms of pharmacy management and pharmaceutical care services.

MATERIALS AND METHODS:

In this study, a questionnaire form was used as data collection tool. The questionnaire consists of four parts. The first part consists of demographic data of community pharmacies. The second part consists of questions about the employees, third part consists of patient counseling duties and the last part consists of administrative duties in community pharmacies. The questionnaire forms were sent to pharmacists via e-mail. The data obtained; It was also evaluated in SPSS Version 23.0.

RESULTS:

58% of the pharmacists in the study are women and 42% are men. The majority of pharmacies (41.3%) did not have a task distribution among staff. This may cause the pharmacy services to be interrupted. Half of the pharmacists (50.0%) stated that they do not inform their patients about traditional and alternative therapies. On the basis of this, pharmacists may feel that they are inadequate on this issue or they may be opposed to traditional and alternative treatment or they may not have enough time to advise on this issue.

CONCLUSIONS:

With the determination of workload and workflow in community pharmacies, the quality of community pharmacy services can increase.

ACKNOWLEDGEMENT

This study has no financial supporters.

REFERENCES:

1. The Role of Pharmacist in the Healthcare System. World Health Organization, 1994.
2. Angelo LB, Christensen DB, Ferreri SP (2005). Journal of American Pharmacist Association. 45:138-144.

P-172: DIETARY SUPPLEMENT REGULATIONS IN TURKEY AND COMPARISON WITH USA, EU AND JAPAN LEGISLATIONS

Kartal, ME., Ozcelikay, G.,

Ankara University, Faculty of Pharmacy, Department of Pharmacy Management, Ankara, Turkey

INTRODUCTION:

Adam Smith, the writer of the Wealth of the Nations, says that the architecture of the politics in society is the merchants and manufacturers (1). As his sentence applied to nowadays the legislations of the governments get in shape through the sectors. One example of this condition is the dietary supplement sector which took in form in 1990s and expanded to other countries after that via its own legislation changes in each government. Dietary supplements are the most popular formulas which are consumed and thought to be safe by most of people in order to maintain health conditions and get enough nutrition due to lower nutrition levels of foods. However natural does not mean safe and dietary supplements can interact with most of medications which can result adverse effects. Thus legislations associated with dietary supplements are important for public health.

MATERIALS AND METHODS:

This research is a descriptive study consists of literature and legislation review associated with dietary supplements in Turkey and comparison with USA, EU and Japan regulations. In this paper, DSHEA (Dietary Supplement Health Education Act) of USA, Directive 2001/83/EC and Directive 2004/24/EC of European Union and regulations of Japan Health and Food Association were investigated to compare dietary supplement policy of Turkey.

RESULTS:

Dietary supplements, in other words food supplements are subject to similar legislations in different countries. Turkish dietary supplement legislation is the most liberalistic and Japan legislation has the most strict rules as compared with EU and

USA. Dietary supplement sector has been growing since 1994. Turkish legislations is the harmonization of USA and EU regulations. Vitamins, minerals, amino acids, probiotics, prebiotics, carbohydrates, proteins, fatty acids and plant origin substances are included in the name of dietary supplements in Turkish legislation (2). Although herbal formulations are evaluated under herbal medicine or traditional herbal medicines in EU, those got approval easily in Turkey. GMP is one of the basic requirement for dietary supplement, however it is recommended in Turkey (3). Adverse effect following and reporting is very important in USA whereas it is not important in Turkey and EU (4). In addition, health claims and advertising of dieatary supplements is very liberalistic as in USA, on the other hand it is very strictly controlled in Japan (5).

CONCLUSIONS:

Turkey imitates the legislations of developed countries. However through globalization each countries' legislations become similar to each other. Also legislations of developed countries does not always mean the best legislation. So, Turkish legislation is urgently needed to be reevaluted.

REFERENCES:

1. Smith A, The Wealth of Nations, Capstone; 1 edition (August 30, 2010)
2. Turk Gida Kodeksi Takviye Edici Gidalar Tebligi, Resmi Gazete, 16 Agustos 2013, 28737
3. Directive 2004/24/EC
4. LeDoux MA et al., (2015). European Journal of Nutrition, 54:1-8
5. http://www.mhlw.go.jp/english/topics/foodsafety/fhc/index.html (last accessed on:11/03/2018)

P-173: A STUDY ON PHARMACOECONOMIC EVALUATIONS AND THE ETHICAL APPROACH OF THE TURKISH PHARMACEUTICAL INDUSTRY TO THIS SUBJECT

[1] Oral, M., [2] Ozcelikay, G.

[1] Ministry of Health, Turkish Medicines and Medical Devices Agency, Ankara, Turkey

[2] Ankara University, Faculty of Pharmacy, Department of Pharmacy Management, Ankara, Turkey

INTRODUCTION:

Pharmacoeconomics is a scientific discipline handling the comparison of drugs used for prevention, diagnosis, and treatment of diseases within the scope of economy and efficiency (1). For making comments according to the results being reached by using the findings obtained, extrapolation of them may be required. Pharmacoeconomic modeling methods have been developed according to this need (2). Ethics refers to the moral judgments of a person concerning right and wrong (3). The aims of this study are to determine the usage rates of pharmacoeconomic evaluation methods by the Turkish Pharmaceutical Industry (TPI) and to investigate ethical approach of the TPI while using these methods.

MATERIALS AND METHODS:

In this study, the questionnaries were held regarding the pharmacoeconomics and ethics to the TPI. According to the findings obtained from questionnaires, usage rates of pharmacoeconomic analysis and modelling methods in TPI are discussed by considering the ethical approach.

RESULTS:

It is determined that pharmacoeconomic evaluations are not performed at high rate in the TPI and pharmacoeconomic analysis methods are used higher than the modeling methods, the most used pharmacoeconomic analysis method is the cost-effectiveness analysis and the most used modeling method is the decision analysis in the TPI and there is a lack of information on pharmacoeconomic modeling methods in TPI and these methods are mostly not used.

CONCLUSIONS:

The TPI needs training in pharmacoeconomics and ethical issues and does not attach high importance to the ethical principle of beneficence which is one of the basic ethical principles within the scope of pharmacoeconomic evaluations.

REFERENCES:

1. Ilbars H, Ozcelikay G (2011). Turkish Journal of Pharmaceutical Sciences, 8(3):219-226.
2. Yalcin-Balcik P, Sahin B (2013). Hacettepe Sağlık İdaresi Dergisi (Hacettepe Journal of Health Administration), 16(2):121-134.
3. Vadastreanu et al., (2015). Procedia Economics and Finance, 26:1068-1073.

P-174: ATTITUDE SCALE DEVELOPMENT STUDY FOR DRUG SIDE EFFECT PICTOGRAMS.

Tarhan, N., Arslan, M., Sar, S.

Ankara University, Faculty of Pharmacy, Department of Pharmacy Management, Ankara, Turkey

INTRODUCTION:

Drug pictograms are tools that help both health professionals and patients to understand and read drug related information easier (1). In the literature, there are some studies examining drug pictograms, however to the best of the authors' knowledge, a study in pharmacy field has not been found in Turkey. To fill this gap, the attitude scale for drug side effect pictograms was developed.

MATERIALS AND METHODS:

This study was conducted with the 5th class pharmacy students in Ankara University (n=70). The proposed scale consists 20 items related to attitudes towards drug side effect pictograms prepared with 5 point Likert Scale [(1) Absolutely disagree to (5) Absolutely agree]. The content validity ratios developed by Lawshe (1975) were used in determining the content validity of the scale (2), and the number of items decreased to 13. Exploratory factor analysis (EFA) and confirmatory factor analysis (CFA) were conducted via SPSS 18.0 and LISREL 8.80 package programs for reliability and validity of the scale.

RESULTS:

As a result of the analysis, 3 items were extracted from the 13-item scale and the KMO value was calculated as 0.817. As a result of EFA, it was found that the one-factor structure explained 53.367% of the total variance. The Cronbach alpha value of the scale was 0.896. This value indicates that the reliability of the developed scale is high. CFA showed that the one-dimensional structure of the scale was valid and goodness of fit indexes for the CFA model were in acceptable levels.

CONCLUSIONS:

The “drug side effect pictogram attitude scale” was found reliable and valid by this study. This scale can be applied to the community or hospital pharmacists for future studies.

ACKNOWLEDGEMENTS:

Authors want to thank to the students participated in this study.

REFERENCES:

1. Hämeen-Anttila K, Kemppainen K, Enlund H, Patricia JB, Marja A. (2004). Patient education and counseling, 55(3):371-378.
2. Lawshe CH (1975). Personnel Psychology, 28:563-575.

P-175: KNOWLEDGE AND ATTITUDE OF COMMUNITY PHARMACY PERSONNEL ABOUT IMPLEMENTING OF THE PHARMACEUTICAL TRACK & TRACE SYSTEM

[1] Sayar, A., [2] Erdogan, ON., [3] Akbal Dagistan, O., [4] Erdogan MS.

[1] Istanbul University, School of Pharmacy, Istanbul, Turkey

[2] Istanbul University, School of Pharmacy, Department of Pharmacy Management, Istanbul, Turkey

[3] Istanbul University, School of Pharmacy, Department of Pharmaceutical Technology, Istanbul, Turkey

[4] Istanbul University, School of Medicine, Department of Public Health, Istanbul, Turkey

INTRODUCTION:

Pharmaceutical Track & Trace System is a successful implementation of Track & Trace approach which has been applied since 2010 on the pharmaceutical field in Turkey. Briefly, it defines the infrastructure framework for all units/single pack belonging to each pharmaceutical product in Turkey and works by using the Datamatrix code, which provides the sureness of the uniqueness of the units (1). The system gathers main shareholders of pharmaceutical Industry, as pharmaceutical companies, pharmacy warehouses, pharmacies and social security institution, who have in part in the product life cycle of the drug and share the responsibility, together (2,3). Aim of this study was to evaluate the community pharmacy personnel’s attitudes and knowledge about the Pharmaceutical Track & Trace System in order to reveal their expectations and identify their problems about the system.

MATERIALS AND METHODS:

Community pharmacies located in Beyoglu district of Istanbul were included into the study (n=120). The personnel were voluntarily conducted in the study by the permission of the Istanbul Chamber of Pharmacy. 56 pharmacies participated in the study. The data were collected from 15th of April to 30th of April 2017 by using a structured questionnaire. The study is cross-sectional and qualitative.

RESULTS AND DISCUSSION:

44 % of the attendees were female, 56 % male, respectively. The average age of the personnel was 35.5 and their average of service year was 15.14. 86 % of personnel described that the system was useful in terms of counterfeit drugs, expired drugs, and smuggling of drugs. While 57% percent of attendees thought that the system provides an advantage for the patients about reach drugs, only 37 % of personnel said a positive effect of the system on the availability

of the drugs on the market. 71% of personnel stated that the positive contribution of the system to the withdrawal process of drug. Consequently, Pharmaceutical Track & Trace System is useful in terms of drug safety/patient and withdrawal process of a drug from the market. On the other hand the system needs to be simplified and the infrastructure process should be improved.

REFERENCES:

1. https://www.its.gov.tr/index.php accessed 23.03.2018
2. http://www.titck.gov.tr/Ilac/ITS accessed 23.03.2018
3. Altunkan SM, Yasemin A, Aykac İT, Akpinar E (2012). Health Informatics and Bioinformatics (HIBIT), 2012 7th International Symposium, pp 24-30.

P-176: PERCEPTION OF GENERAL SELF EFFICACY AND OCCUPATIONAL COMMITMENT OF ACADEMIC PERSONNEL WHO IS WORKING AT ANKARA UNIVERSITY FACULTY OF PHARMACY

Kilicdagi Y., Ozcelikay G.

Ankara University, Faculty of Pharmacy, Department of Pharmacy Management and History, Ankara, Turkey

INTRODUCTION:

Universities are organizations that pursue their existence through research, learning and teaching activities. Academicians are also the main actors of these organizations in terms of organizational, educational and psychological aspects such as mutual interaction, motivation, professional commitment, self-efficacy, and productivity. In this study, the relationship between academicians' self-efficacy perceptions and occupational commitment was examined.

MATERIALS AND METHODS:

The sample of the research consists of 46 academicians working at the Faculty of Pharmacy of Ankara University. The data obtained in the study were collected by applying a questionnaire to the sample size. Surveys contains the basic demographic questions with general self-efficacy scale and three-dimensional scale occupational commitment. In the analysis of the data, descriptive statistical tools and t-test and one-way ANOVA and Pearson correlation analysis were used.

RESULTS:

When the demographic characteristics of the academicians participating in the research are examined; Of 73.8% were female, 21.7% male, 84.8% married, 15.2% were found to be the single. It was found that general self-efficacy perceptions of male academicians were higher than female academicians, while the general self-efficacy perceptions of academicians were found to be significant and positive effect on their level of occupational commitment.

CONCLUSIONS:

In this study, the general self-efficacy perceptions of academicians were found to be high. At the same time, it was found that there was a significant relationship with professional commitment levels. It is thought that all the results of the study will contribute to the literature of both education and management.

REFERENCES:

1. Tolentino RC (2013). International journal of Information technology and Business Management, 15(1):51-59.
2. Bandura, A (2006). Self-efficacy beliefs of adolescents, 5(1):307-337.
3. Bong M, Skaalvik EM (2003). Educational psychology review, 15(1):1-40.

P-177: PREDICTION OF BIORELEVANT PKA VALUES OF SOME AMPHOTERIC DRUGS FROM THEIR PKA AT 25˚C BY USING ABRAHAM'S DESCRIPTORS

Sogut, O., Ortak, H., Cubuk Demiralay, E., Alsancak, G.

Süleyman Demirel University, Arts and Science Faculty, Department of Chemistry, Isparta, Turkey

INTRODUCTION:

A large proportion of organic molecules relevant to medicine contain one or more ionizable groups, which means that fundamental physical and chemical properties depend on pH of the solution via the corresponding ionization constant (pKa) values of the molecules. However, for many compounds experimental pKa values are not available, and for others the measured values are sometimes uncertain. In practice, the common reference value is 25°C and reported pKa values are mainly clustered around room temperatures. There is limited number of study at biorelevant temperature (37°C).

MATERIAL:

In this study, aqueous pKa values for some cephalosporins (2.10-3 M) were determined by potentiometric method. Mettler Toledo MA 235 pH/ion analyzer system were used for pH measurements. pKa values were deduced graphically form Bjerrum plots by using Solver aproach. Moreover aqueous pKa values of some amphoteric sulfonamides (1.10-5 M) were determined by spectrophotometric method. The UV-Vis spectra were recorded at each pH using Perkin Elmer LAMBDA 20. The cell was thermostated at 25±0.5 0C.

RESULTS:

Acidity constant is a very important property of drug candidates, because it is of main importance for their ADME properties. In this study, pKa values of some amphoteric drugs were determined by using potentiometric and spectroscopic methods. We have developed a computational method for estimating biorelevant pKa using a quantitative structure property relationship (QSAR) approach. The Abraham's five LFER solvation descriptors (E, S, A, B, V values) were considered as molecular descriptors. In the present study, the difference between their pKa values at 25˚C and 37˚C for some amphoteric drugs were predicted by using special equation. The biorelevant pKa values of amphoteric drugs were calculated by fitting the molecular descriptor equation to their pKa at 25˚C.

CONCLUSION:

Values of the ionization constants at 37°C, are more meaningful for interpreting mechanisms of cellular transport by ionizable molecules. A simple equation for predicting the biorelevant pKa from knowledge of the value at 25°C was derived. This investigation is expected to be a useful contribution, since pKa determinations are scarcely reported at 37°C.

P-178: PREDICTION OF RETENTION BEHAVIOUR OF SOME NSAIDS: RELATION BETWEEN CHROMATOGRAPHIC DATA AND ABRAHAM SOLUTE DESCRIPTORS

[1] Cubuk Demiralay, E., [1] Sogut, O., [2] Secilmis Canbay, H., [1] Ortak, H., [1] Alsancak, G.

[1]Suleyman Demirel University, Arts and Science Faculty, Department of Chemistry, Isparta, Turkey

[2]Mehmet Akif Ersoy University, Department of Bioengineering, Burdur, Turkey

INTRODUCTION:

Non-steroidal anti-inflammatory drugs (NSAIDs) are a class of weak acidic compounds which cover a number of different chemical types. Reversed phase liquid chromatography (RPLC) is one of the most powerful analytical methodologies used for quantitative determination of these compounds. Quantitative structure retention relationships play an important role in enhancing the quality of chromatographic method optimisation. Molecular descriptors are numerical values that characterize the properties of molecules. It is possible to investigate retention behaviour of solutes in RPLC employing Abraham solvation parameters. The Abraham solute parameters (E, S, A, B and V) and Abraham equation coefficients (c, e, s, a, b and v) represent the extent of all known interactions between solute, mobile phase and stationary phase.

MATERIALS AND METHODS:

The chromatographic analysis of the analytes was performed using an isocratic system. Effect of percentage of organic modifier (acetonitrile-water binary mixture containing 25 mM phosphoric acid; pH range 2.5-7.0) were investigated on retention in RP column using solvation parameter model. A Nucleosil 300-5 C4 RP column (25 cm×4.6 mm, 5µm) was used for the analysis. This study was performed at 37oC. Gemini C6 phenyl analytical column was also used for chromatographic studies at 25°C.

RESULTS:

In the present study, quantitative structure-retention equation describing relations between the solute descriptors of some NSAIDs (etodolac, tolmetin, ketorolac, deksketoprofen, diclofenac, ketoprofen, naproxen, ibuprofen, flurbiprofen) and their chromatographic behaviour were derived. To quantitatively characterize the structure of the analytes the following five structural descriptors are employed: McGowan volume, the polarizability/ dipolarity, the overall hydrogen bond basicity, the overall hydrogen bond acidity, an excess molar refraction. The constants reflect whether the analyte prefer the interaction with the stationary phase or the mobile phase. Positive values in the regression coefficients indicate that the descriptor contributes positively to the value of capacity factor, whereas negative values indicate that the greater the value of the descriptor, the lower value of log k. It may be concluded that polar interactions have negative effects on retention. Conclusions:This work represents the first study dealing with the reversed phase retention mechanism of some NSAIDs at different proportions of acetonitrile-water binary mixtures.The linear solvation energy relationship (LSER) methodology was used to explain the retention mechanism. The results showed some regularity in retention behaviour of the compounds studied.

P-181: QUANTITATIVE ANALYSES OF DAPAGLIFLOZIN, A SODIUM-GLUCOSE COTRANSPORTER II INHIBITOR, BY DIFFERENTIAL PULSE VOLTAMMETRY

Ates, AK., Erk, N.

Ankara University, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Type II diabetes, which accounts for more than 90% of all diabetes, is a complex progressive metabolic derangement associated with comorbidities such as obesity, hypertension, and hyperlipidemia (1). Dapagliflozin is a stable and highly selective Sodium-glucose cotransporter II (SGLTII) inhibitor. Binding of dapagliflozin to SGLTII inhibits renal glucose reabsorption, promotes urinary glucose excretion,

and thereby lowers hyperglycemia by an insulin-independent mechanism (2).

Herein, for the first time, quantitative analyses of dapagliflozin (DPG) was carried out using voltammetric method.

MATERIALS AND METHODS:

A three electrode cell was employed using an Ag/AgCl as a reference electrode, Pt wire as a counter electrode and a glassy carbon electrode (GCE) as a working electrode. Since DPG exhibits a diffusion-controlled process on GCE, DPG was analysed by differential pulse voltammetry.

RESULTS:

The voltammetric responses of DPG presented a good linearity with an increase in concentration within two concentration ranges of 10–48 μM and 48–100 μM with a low detection limit of 0.41 μM and RSD of % 4.89.

CONCLUSIONS:

In this study, for the first time, a simple, rapid, sensitive and cost-effective electrochemical analyses method was developed for the quantitative determination of DPG and applied to DPG in bulk with satisfactory results. The developed method could be a promising alternative for routine analysis of DPG in real samples.

ACKNOWLEDGEMENTS:

This research was supported by the Ankara University Scientific Research Projects Coordination Unit (Project Numbers: 15B0237001, 15L0237007).

REFERENCES:

1. Grundy SM (2007). Metabolic Syndrome Pandemic, 28:629-636.
2. Bailey et al., (2010). Lancet., 375: 2223-2233.

P-182: INDUCED DUAL WAVELENGTH SPECTROPHOTOMETRIC METHOD FOR THE SIMULTANEOUS ANALYSIS OF NEBIVOLOL AND AMLODIPINE IN BULK AND THEIR MIXTURES

[1] Erk, N. [1] Ates, AK.

Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Hypertension, also known as high or raised blood pressure, is a condition in which the blood vessels have persistently raised pressure. Amlodipine (AML) is a potent dihydropyridine calcium antagonist useful in the management of angina pectoris and hypertension. Nebivolol hydrochloride (NEB) is a beta adrenergic blocker. It selectively blocks the β1-adrenoceptor (1,2).

MATERIALS AND METHODS:

Induced dual wavelength spectrophotometric method is applied for the simultaneous determination of two active ingredients in mixture with complete overlapped zero order spectra at two wavelengths.

RESULTS:

The proposed method is the application of induced dual wavelength method where the linearity range and percentage recoveries for AML , and NEB were 5.0 -35.0 ug/ml and 100.05 ± 1.11 ,99.05 ± 0.89, respectively. The absorbance of the zero order spectra at 237.53 and 287.41 nm (equality factor was found as 9.22) for AML and 281.46 and 266.30 nm (equality factor was found as 18.14) for NEB were measured .

CONCLUSIONS:

The proposed method permit simple, rapid, and direct determination of binary mixtures without previous separations. Moreover, it has many advantages over other separation techniques such as high-performance liquid chromatography or gas chromatography.

ACKNOWLEDGEMENTS:

This research was supported by the Ankara University Scientific Research Projects Coordination Unit (Project Numbers: 15B0237001, 15L0237007).

REFERENCES:

1. Hemdan A (2016). Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 164:52-60.
2. Dhandapanı B, Thirumoorthy N, Prakash DJ (2010). E-Journal of Chemistry, 7(2); 341-348.

P-183: DETERMINATION OF GRANISETRON IN PHARMACEUTICAL PREPARATIONS BY CE-DAD

[1] Ozyurek, B., [1] Cecen, SD., [2] Dal, AG.

[1]Anadolu University, Graduate School of Health Sciences, Eskisehir, Turkey

[2]Anadolu University, Department of Analytical Chemistry, Eskisehir, Turkey

INTRODUCTION:

Granisetron (GRA) is a potent and selective 5-hydroxytryptamine receptor antagonist with antiemetic activity indicated for prevention and treatment of nausea and vomiting associated with cytotoxic chemotherapy and radiotherapy, and postoperative nausea and vomiting (1). The aim of the study is to develop a rapid and sensitive capillary electrophoretic (CE) method for the determination of GRA in pharmaceutical preparations.

MATERIALS AND METHODS:

All chemicals used were analytical grade. An Agilent 7100 model CE with DAD (205.5 nm) was used for CE experiments. Separation was achieved by a fused silica capillary with 40 cm effective (48.5 cm total, 75 µm i.d.) length. The run buffer was composed of 20 mM phosphate buffer (pH 2.75) and applied voltage was 22.5 kV. Metoprolol was used as IS.

RESULTS:

All parameters effecting separation were investigated. Under optimum conditions the migration times for GRA and IS were 6.71 min and 6.94 min, respectively. The method was validated for linearity, precision, accuracy, sensitivity, stability, specificity and robustness. The LOQ was found to be 4.30×10-7 M. The developed and validated method was successfully applied to GRA tablets and ampoules containing 1 mg and 3 mg/mL GRA, respectively.

CONCLUSIONS:

The CE method proposed here is rapid, sensitive and specific. The method was applied to pharmaceutical preparations of GRA and the contents were found to be in the limits of USP39 (2). This method is proposed for the routine analysis of GRA.

ACKNOWLEDGEMENTS:

This study was supported by Anadolu University Scientific Research Projects Commission under the grant no: 1505S428.

REFERENCES:

1. Heda AA et al., (2011). Indian Journal of Pharmaceutical Sciences, 73 (6): 696-699.
2. U.S. Pharmacopeia National Formulation 39 (2016). The National Formulary 34, Rockville: United States Pharmacopeial Convention.

P-184: DEVELOPMENT AND VALIDATION OF A NEW HPLC METHOD FOR QUANTITATIVE ESTIMATION OF CEFTIOFUR IN VETERINARY SUSPENSIONS

[1] Geven, A., [2,3] Ozcan, S., [3,4] Levent, S., [2,3] Can, NO.

[1]Anadolu University, Faculty of Pharmacy, Eskişehir, Turkey

[2]Anadolu University, Faculty of Pharmacy, Department of Analytical Chemistry, Eskisehir, Turkey

[3]Anadolu University, Faculty of Pharmacy, Doping and Narcotic Compounds Analysis Laboratory, Eskisehir, Turkey

4Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskisehir, Turkey

INTRODUCTION:

Ceftiofur (CEF) is a third-generation semi-synthetic cephalosporin antibiotic, which is licensed for use in veterinary medicine (1). The aim of this study was to develop a fast and reliable HPLC method for determination of CEF in veterinary suspensions. Analysis of CEF and benzocaine (internal standard, IS) was performed using a fused core silica column.

MATERIALS AND METHODS:

Analyses were performed using a Prominence series of HPLC instrument from Shimadzu (Japan). A C18 bonded fused-core silica particle column (2.7 µm particle size, 10x4.6 mm from Supelco) was used for separation. The mobile phase, which was pumped at the rate of 1.0 mL/min, was consisted of acetonitrile: phosphate buffer (0.025 M, pH 2.4): water (28:10:62, v/v/v). The analytes were detected at 289 nm by using a PDA detector. A simple sample preparation step was applied, in which only dissolution in THF-ACN mixture, subsequent dilution and filtration through 0.22-µm PTFE filter steps are required; 1000 µL of the resulting solution was spiked with 200 µL 1.87x10-4 M IS solution prior to injection. The validity of the method was verified according to ICH guidelines using quality control solutions (2).

RESULTS:

The method was linear in the range of 1.98x10-8 M - 0.97x10-5 M (y= 310801x - 0,0088; R2 =1.000). LOD and LOQ of the method were 1.76x10-7 M and 5.85x10-7 M, respectively. The developed method permits quantitative determination of CEF in pharmaceutical suspensions with high accuracy and precision.

CONCLUSIONS:

The method proposed in this study was found to be applicable for fast analysis of CEF in veterinary preparations. This is the first study in which a fused-core column was utilized for the analysis of CEF in veterinary preparations.

ACKNOWLEDGEMENTS:

Authors would like to acknowledge Anadolu University Scientific Research Projects Commission for financial support (Project No: 1606S567) and VET. Hüseyin OZCAN from Eskisehir Branch of the Republic of Turkey Ministry of Food, Agriculture and Livestock for kind support in sample preparation.

REFERENCES:

1. Hornish RE, Kotarski SF (2002). Current Topics in Medicinal Chemistry, 2: 717–731.
2. ICH Harmonised Tripartite Guideline (2005). Validation of Analytical Procedure Text and Methodology Q2 (R1).

P-185: GREEN HPLC USING ECO-FRIENDLY ETHANOL BASED MOBILE PHASES IN PHARMACEUTICAL ANALYSIS

Dogan, A., Eylem, CC., Basci, N.

Hacettepe University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Green analysis techniques based on solvent consumption and substitution are the two major applications in greening chromatographic analysis. Decreasing the toxicity of solvents used in mobile phases by substituting them with less or non-hazardous ones or revealing the consumption amounts by using lower diameter columns or miniaturizing instruments are a fact that can be implemented to an analysis (1, 2). Environmentally friendly water and ethanol based mobile phases reduce the use of toxic solvents such as methanol and acetonitrile, and consequently the necessary cleaning of waste is reduced. In the presented study, ethanol having less toxic and hazardous effects has been selected as organic modifier. Famotidin, paracetamol and thiocolchicoside were selected molecules for demonstration of the applicability of green HPLC in pharmaceutical analysis. Famotidine is a histamine H2 receptor antagonist inhibiting stomach acid production. Paracetamol is a medication used to treat pain and fever. Thiocolchicoside is a muscle relaxant with anti-inflammatory and analgesic effects.

MATERIALS AND METHODS:

Experiments were carried out using an LC system connected to a Shimadzu LC–DAD (at 254 nm). HiChrom Nucleosil C18 (150 × 4.6 mm, 5 µm) and C8 (150 × 4.6 mm, 5 µm) analytical columns were tested as stationary phases. In the mobile phase optimization, EtOH and phosphate buffer contents were adjusted to the desired concentrations for the elution of selected analytes both in isocratic and gradient elution modes. İnitial flow rate of the mobile phase was set to 1.0 mL/min and the injection volume was 20 µL.

RESULTS:

Developed mobile phase was consisted of NaH2PO4 (50 mM, pH:4.6) + EtOH (95:5, v/v) in gradient elution mode. Famotidin, paracetamol and thiocolchicoside were well separated both form baseline and each other with the capacity factors of 2.14, 2.53 and 4.26 min, respectively. The developed EtOH based mobile phase in RP-HPLC was validated in terms of ICH requirements (3) and found to be accurate, precise, repeatable, rugged and robust. Developed method was also successful in pharmaceutical analysis of famotidin, paracetamol and thiocolchicoside from Turkish drug market.

CONCLUSIONS:

Our objective in this study is to evaluate chromatographic behaviors of api's in terms of green mobile phase. The usage of buffer much more than the organic phase shows that this kind of analysis can be performed using more aqueous phases. The findings of the presented study suggested that environmentally friendly ethanol and water based mobile phases can successfully apply in the pharmaceutical analysis.

REFERENCES:

1. Welch CJ et al., (2010). TrAC Trends in Analytical Chemistry, 29 (7): 667-680.
2. 2. Gałuszka A, Migaszewski Z, Namieśnik J (2013). TrAC Trends in Analytical Chemistry, 50:78-84.
3. 3. Guideline IHT (2005). Validation of analytical procedures: text and methodology, Q2 (R1), 1.

P-187: HPLC DETERMINATION OF EPIRUBICIN IN NANOPARTICULATE DRUG DELIVERY SYSTEM

[1] Gencer, A., [1] Duraloglu, C., [2] Kocak, E., [2] Celebier, M., [1] Arica Yegin, B.

[1]Hacettepe University, Faculty of Pharmacy, , Department of Pharmaceutical Technology, Ankara,Turkey

[2]Hacettepe University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara,Turkey

INTRODUCTION:

Epirubicin is an anthracycline drug used for chemotherapy. It can be used in combination with other medications to treat many cancers including lung cancer (1). There are some HPLC methods reported in the literature for the analysis of epirubicin in its pharmaceutical dosage forms and biological materials (2-4). However, none of these methods are sensitive and specific for the determination of epirubicin in nanoparticulate drug delivery system. Therefore, an HPLC method for epirubicin was developed and validated.

MATERIALS AND METHODS:

In this work, an ACE C18 column (250 x 4.6 mm, 5µm) was used for separation of epirubicin from nanoparticulate system matrix components. Acetonitrile and phosphate buffer (25 mM pH: 3.0) 40:60 mixture was used as mobile phase. Flow rate was 1.0 mL/min and detection wavelength was 234 nm. Injection volume was 20 µL where column was in ambient temperature.

RESULTS:

Epirubicin was successfully determined in the presence of matrix components coming from nanoparticulate drug delivery system. Total analysis was shorter than 12 minutes. The method was

validated according to the guidelines and found that it is precise, accurate, sensitive for determination of epirubicin in the prepared nanoparticulate system.

CONCLUSIONS:

Although there are various analytical techniques for determination of epirubicin in pharmaceutical dosage forms and biological materials, a specific method was developed for determination of epirubicin in nanoparticulate formulation. The analytical method was successfully applied for investigation of the encapsulation efficiency and drug release profile of epirubicin.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Hacettepe University Scientific Research Programs (Project number: TSA-2018-16747)

REFERENCES:

1. Minott Gi, Menna P, Salvatorelli E, Cairo G, Gianni L (2004). Pharmacological Reviews, 56 (2):185-229
2. Gong Xl et al., (2008). West China Journal of Pharmaceutical Sciences, 23(1):68.
3. Lifen T, Bingyan T, Jueheng W, Huihua C, Hongying C (2001). Guangdong, 4:020.
4. Kurbanoglu S et al.,(2014). Journal of Liquid Chromatography & Related Technologies, 37(11):1583-96.

P-188: PREPARING A NEW BIOSENSOR FOR HYPOXANTHINE DETERMINATION

[1] Gorgulu, M., [1] Kabasakal, DC., [2] Akin, D.,[2] Cete, S., [1] Yasar, A.,

[1]. Gazi University, Institute of Sciences, Department of Chemistry, 06500 Ankara, Turkey

[2]. Gazi University, Faculty of Sciences, Department of Chemistry, 06500 Ankara, Turkey

INTRODUCTION:

Hypoxanthine accumulates in biological tissues as the main product of the degradation of adenine nucleotides in biological materials. The concentration of inosine and / or hypoxanthine can be used as a fish freshness determinant. The amount of hypoxanthine available is often used in the detection of meat freshiness in the food industry and in some pathological processes in the human body. Therefore, the quantification of hypoxanthine content is important for the quality control of fish and other fish products in the food industry.

MATERIALS AND METHODS:

Polypyrrole-polyvinylsulphonat films have been prepared on the platinum electrode by the electropolymerization of pyrrole was carried out in the presence of polyvinylsulphonate. Optimum conditions of polypyrrole-polyvinylsulphonate film was determined. Xanthine oxidase and uricase enzymes have been immobilized in polyanpyrrole-polyvinylsulphonate via the entrapment method. The linear working range of biosensor for hypoxanthine was determined. The effects of pH and temperature on the response of the hypoxanthine biosensor were investigated. Reusability and storage stability were determined of the biosensor.

RESULTS:

Linear working range of prepared enzyme electrode was determined 1 µM to 10 mM. The prepared enzyme electrode maintains 74.5% of its performance at the end of 20 measurements. The values of Km and Vmax for the Pt / PPy-PVS / KO-U enzyme electrode system were found to be 3.7 µM and the 0.19 µA / min respectively. The optimum pH and temperature values for the enzyme electrode system were found to be 8.2 and 30 °C.

CONCLUSIONS:

Electrochemical studies show reliable and good results over very low concentration ranges. This method is relatively fast and cheap compared to other methods.

REFERENCES:

1. Devi R, Thakur M, Pundir CS (2011). Biosensors and Bioelectronics, 26(8):3420-3426.

P-189: STABILITY-INDICATING HILIC METHOD FOR THE DETERMINATION OF SOME ANTIVIRALS FROM THEIR PHARMACEUTICAL DOSAGE FORMS

[1] Erkmen, C., [2] Gumustas, M., [1] Ozkan, SA.,[1] Uslu, B.

[1]Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

[2]Ankara University, Institute of Forensic Sciences, Department of Forensic Toxicology, Ankara, Turkey

INTRODUCTION:

Nucleoside and nucleotide reverse transcriptase inhibitors are synthetic nucleoside and nucleotide analogs used for the treatment of viral infections. In HIV-infected patients, combined therapy of the lamivudine, zidovudine and abacavir shows superior efficacy compared to single therapy. Hydrophilic interaction liquid chromatography (HILIC) is an interesting alternative for the analysis of polar substances. It can be defined as a separation method that combines stationary phases usually used in normal phase method and mobile phases used in reversed phase separations. Main advantages of HILIC is the efficient retention and separation of polar compounds, which is difficult to achieve using reversed phase condition. The aim of this study is to demonstrate of a HILIC method for the simultaneous, determination of abacavir, lamivudine, and zidovudine.

MATERIALS AND METHODS:

Agilent 1100 series LC system, equipped with a diode array detector was used for analysis. Analysis have been realized with the Kinetex HILIC (150 mm x 4.6 mm, 2.6 µm), analytical column, the mobile phase consists of acetonitrile: ammonium acetate buffer solution, 80:20 (v/v) at 25°C. Detection wavelength was selected as 280 nm. Forced degradation studies were carried out by using tablet form. The degradation studies were performed under certain conditions included acid hydrolysis, base hydrolysis, oxidation, UV light exposure at 254 nm, heating in the oven at 80°C and keep the solution in water bath at 80°C. The results were compared to the untreated tablet solution.

RESULTS:

Degradation studies were carried out to examine the selectivity of the analytical method. Tablet sample was subjected to light stress conditions such as (acid hydrolysis with 0.1 M HCl, base hydrolysis with 0.1 M NaOH, oxidation with 0.3% H2O2). It was observed that the degradation products did not interfere with the active substances in 6 different degradation conditions. Therefore, the developed method is suitable for analysis of the active ingredients simultaneously with possible degradation products.

CONCLUSIONS:

As a result of this study, fast, simple, sensitive, selective and fully validated HILIC method has been developed under developed conditions. The proposed rapid and sensitive HILIC method will be readily applicable in quality control laboratories since for simultaneous quantification of abacavir, lamivudine and zidovudine. Thus, the feasibility of the method in complex matrices such as drug samples has also been demonstrated.

ACKNOWLEDGEMENTS:

The authors would like to thank Ankara University Scientific Research Projects Commission for financial support (Project No: 16L0237001).

REFERENCES:

1. Alpert AJ (1990). J. Chromatogr. 499: 177

P-190: INVESTIGATION OF MICROBIOLOGICAL PROPERTIES OF SOME NEW GENERATION SOLVENTS

[1] Dogan Calhan, S., [2] Ulger, M., [3] Efeoglu, C., [3] Dincer Kaya, FN.

[1]Mersin University, Faculty of Pharmacy, Department of Pharmaceutical Biotechnology, Mersin,Turkey

[2]Mersin University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Mersin,Turkey

[3]Mersin University, Faculty of Pharmacy, Department of Analytical Chemistry, Mersin,Turkey

INTRODUCTION:

Deep Eutectic Solvents (DESs) are known as the new generation and green solvents. Because of their polarity and ability to form hydrogen bonds, DES make excellent solvents, meaning that they can dissolve many different kinds of molecules. Moreover, they are defined as environmental friendly because of their low toxicity and they are also biodegradable and biocompatible (1). Due to these properties, deep eutectic solvents are used in many different areas. Especially studies aiming to seriously increase the solubility of medicines, with solubility problems compared to water, are particularly promising according to preclinical studies (2).

On the other hand, when the literature was examined it was seen that there were not enough studies on this topic. For this purpose different DESs were prepared and characterizations were performed and antibacterial activities were determined.

MATERIALS AND METHODS:

Characterization of the different DESs were performed by the Fourier Transform Infrared (FTIR) Spectrometry and the Nuclear Magnetic Resonance (NMR) Spectrometry. The Resazurin Microplate method was used to determine antibacterial activity.

RESULTS:

The DESs used in the study were clarified. Antibacterial activity assays were investigated for five different bacteria and MIC (minimum inhibitory concentration) values were calculated.

CONCLUSIONS:

According to the results, DESs showed low antibacterial activity compared to ampicillin. Taking into account the interesting applications of the pharmaceutical industry, in addition to other industries, a large number of DESs have been concluded to be able to expand their work by investigating more physicochemical, antibacterial and cytotoxic properties of DES.

REFERENCES:

1. Tang B, Row KH (2013). Monatsh. Chem., 1427–1454.
2. Morrisona HG et al., (2009). Int. J. Pharm, 378: 136–139.

P-191: A GREEN EXTRACTION METHOD FOR QUANTIFICATION OF PHENOLIC SPECIES FROM OLIVE FRUITS

[1] Efeoglu, Ç., [1] Dincer Kaya, FN., [2] Dogan Calhan, S.

[1]Mersin University, Faculty of Pharmacy, Department of Analytical Chemistry, Mersin,Turkey

[2]Mersin University, Faculty of Pharmacy, Department of Pharmaceutical Biotechnology, Mersin,Turkey

INTRODUCTION:

Recently, deep eutectic solvents (DESs) were introduced as a green alternative to conventional solvents for sample preparation and extraction procedures. A deep eutectic solvent is consist of an eutectic mixture of two solid and has a lower melting point than its components (1). DESs are biodegradable, non-toxic, non-volatile, non-flammable, inexpensive, and easily accessible and environmentally friendly (2,3). In this study, we aimed to develop a new procedure to extract fenolic species from olive fruits using deep eutectic solvents. For this purpose, choline chloride -urea mixture was used as DES.

MATERIALS AND METHODS:

The synthesized DES were characterized by Fourier transform infrared spectroscopy (FT-IR). After extraction of the olive fruits which planted in Mersin region, phenolic substances were determined by High-Performance Liquid Chromatography with Diode-Array Detection (HPLC/DAD).

RESULTS:

Concentrations of vanillin, vanillic acid, 2,3-dihydroxybenzoic acid and 4- hydroxybenzoic acid concentrations were determined in the olive fruit samples. Recovery, limit of detection (LOD) and limit of quantification (LOQ) values were calculated for each phenolic species.

CONCLUSIONS:

Results of studies have shown that DESs can be suggest as a green alternative to conventional solvents for extraction of phenolic species from olive fruits.

ACKNOWLEDGEMENTS:

This study was supported by the Scientific Research Projects of Mersin University (Project number: 2017-1-TP2-2223)

References

1. Ongor G, Demiralp B (2014). Orbital., 3:57-60.
2. Zhang Q, Vigier KDO et al., (2012). Chem.Soc. Rev., 41:7108-7146.
3. Yılmaz E, Soylak M (2015). Talanta, 136:170–173.

P-192: DETERMINATION OF ANTAZOLINE, NAPHAZOLINE, EPHEDRINE, CHLORBUTANOL IN PHARMACETICAL POMADE USING RP- HPLC

Kanbes Dindar, C., Günden Göğer, N.

Gazi University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Antazoline (ANT) is a histamine H1 receptor antagonist(1). Ephedrine (EPD) is used to excite the central nervous system, and is also used as decongestant(1). Naphazoline (NPZ) is a sympathomimetic agent and decongestant(1). Chlorbutanol (CLO) is a chemical preservative, sedative hypnotic and weak local anaesthetic(1). These four compounds are pharmacologically active constituents found in pomade. There have been numerous publications describing various methods for the quantification of these compounds individually and in combination with other drugs(2,3). However, literature survey reveals that no method has been reported for determination of ANT, NPZ, EPD and CLO, simultaneously. This study involves the development of reversed-phased chromatographic method for simultaneous determination of ANT, NPZ, EPD and CLO present in a pharmaceutical pomade.

MATERIALS AND METHODS:

Stock solutions of ANT, NPZ, EPD and CLO were prepared in methanol. Standard solutions were prepared from stock solutions by dilution with mobile phase consisted of 10 mM phosphate buffer pH 3 and methanol (80:20, v/v). Shimadzu UV spectrophotometer (UV- 2450) was used for all measurements. The quantification was carried out using an HPLC system (Agilent 1200) with UV detector.

RESULTS:

UV spectra of ANT, NPZ, EPD and CLO(Fig1) indicated that ANT, NPZ, EPD and CLO could not determined by UV spectrophotometry. Optimum chromatographic separations of ANT, NPZ, EPD and CLO have been achieved within 12 minutes at flow rate of 0.6 mL/min by using Agilent Zorbax Eclipse XDB C18 (3.0x75mm, 3.5µm) column and detection was performed at 210 nm. The method was validated in accordance with ICH guidelines. Regression analysis showed good correlations ($R^2 > 0.999$) for ANT in concentration range of 0.05 µg/mL to 100 µg/mL, NPZ in 0.005 µg/mL to 10 µg/mL EPD in 0.166µg/mL to 332 µg/mL and CLO in 1.66 µg/mL to 332 µg/mL.

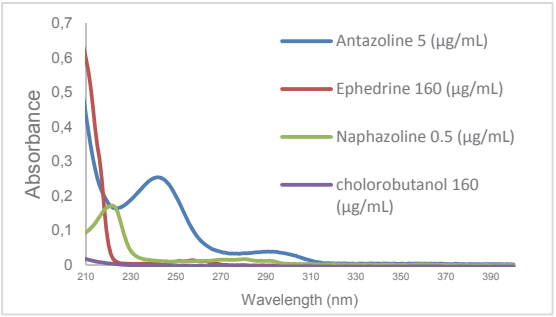


Fig1. UV spectra of ANT, NPZ, EPD and CLO

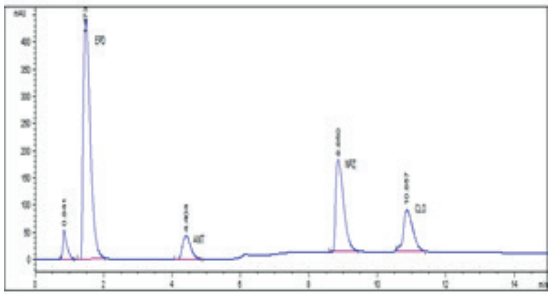


Fig2. HPLC Chromatogram of ANT, NPZ, EPD and CLO

CONCLUSION:

In this study, RP-HPLC method is presented for the determination of ANT, NPZ, EPD and CLO in pomade which offers numerous advantages, such as good resolution, accuracy, precision, selectivity and ease of operation.

REFERENCES:

1. Kayaalp O (1993). Rasyonel Tedavi Yönünden Tıbbi Farmakoloji, Ankara, 1814:2366-2370.
2. Wahbi AM et al., (1978). Journal of Pharmaceutical Sciences, 67:140-141.
3. Abdel Ghani NT et al., (2013). Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 111:131-141.

P-193: OPTIMIZATION OF EXTRACTION PARAMETERS OF REVERSE IONTOPHORETIC DETERMINATION OF BLOOD GLUCOSE IN AN ARTIFICIAL SKIN MODEL

[1] Yengin, C., [2] Der, FG., [2] Sezgin MC., [2] Alcin I., [2] Kilinc E.

[1]Ege University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, İzmir, Türkiye

[2] Ege University, Faculty of Pharmacy, Department of Analytical Chemistry, İzmir, Türkiye

INTRODUCTION:

According to the World Health Statistics 2017 Report (1), published by World Health Organization, an estimated 40 million deaths occurred due to Noncommunicable diseases (NCDs). The majority of such deaths were caused by the four main NCDs, namely: cardiovascular disease, 17.7 million deaths (45% of all NCD deaths); cancer, 8.8 million deaths (22%); chronic respiratory disease, 3.9 million deaths (10%); and diabetes, 1.6 million deaths (4%). For the diagnosis and management of Diabetes mellitus mean fasting plasma glucose (FPG) (mmol/L) level is a golden standard as indicated in the same report (1). For non-invasive glucose monitoring there are 10 technologies present in R&D or marketing level (2). One of the most promising approach among these technologies is reverse iontophoresis (RI). RI is based on the flow of a low electrical current through the skin and glucose measurement is possible because glucose is extracted through the epidermis surface during this convective flow. In this study some experimental parameters are optimized for the RI determination of glucose in an artificial skin model.

MATERIALS AND METHODS:

Methyl cellulose (MC), carboxymethyl cellulose, sodium carboxymethyl cellulose, hydroxypropylmethyl cellulose (Sigma-Aldrich) were used as the electrolyte in the collection chamber. Cellulose ester (CE) membranes with 2000, 12000 and 14000 Daltons MWCO values (Visking) were used as the artificial skins. pH value (pH 1-13) and the ionic strength (7 different combinations) of the extraction medium was investigated. Extraction electrodes distance (1, 2.5, 7 and 10mm) and material (Ag, Pd, Rh, Pt, Ru), extraction potential type (pulse, cyclic, continous) and magnitude (+0.5, +1.0, +1.5 and +2.0V vs Ag/AgCl) and extraction time (3, 12 and 24 hours) were the other parameters employed. During RI procedures extracted glucose samples were quantified by Accu-Chek Active blood glucose monitor (Roche Diagnostics).

RESULTS:

MC gel and CE membrane with 12000 Daltons MWCO combination displayed best responses. Glucose extraction was the highest at physiological pH (pH 7.4) in 0,05M PBS as the optimum ionic strength. Extration electrodes fabricated by electrodeposition of Ag should be located at 7.0mm distance from each other. With a continous potential of +2.0V (chronoamperometric) for 3h, glucose could successfully extracted for 24h.

CONCLUSIONS:

A noninvasive determination method for glucose was developed and optimized. Experimental results were summarized and displayed as tables.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-104S236) and Ege University Department of Scientific Research Projects (BAP, Project numbers: 16/ECZ/007 and 11/ECZ/030)

REFERENCES:

1. http://apps.who.int/iris/bitstream/handle/10665/255336/9789241565486eng.pdf;jsessionid=945CD8DA55E65BD374B-70F11A9160B2E?sequence=1
2. So CF et al., (2012). Medical Devices: Evidence and Research, 5:45-52.

P-194: LC-MS/MS METHOD FOR THE DETERMINATION OF LAMOTRIGINE IN RAT PLASMA AND BRAIN MICRODIALYSATE

[1] Dogrukol Ak, D., [1] Sener, E., [2] Korkmaz, OT.

[1]Anadolu University, Faculty of Pharmacy, Department of Analytical Chemistry, Eskisehir, Turkey

[2]Osmangazi University, Faculty of Medicine, Department of Physiology, Eskisehir, Turkey

INTRODUCTION:

A fast, specific and highly sensitive liquid chromatography tandem mass spectrometry (LC-MS/MS) method for the direct determination of lamotrigine which is an anti-epileptic compound in rat plasma and brain microdialysate has been developed and validated.

MATERIALS AND METHODS:

The analysis was performed on a Supelco Ascentis Express C18 (100x2.1 mm, 2.7 µm particle) core shell column using a binary gradient elution with the mobile phases consisting of acetonitrile and ammonium formate buffer (10 mM). Ionization of the compound was achieved by electrospray ionization (ESI) in positive ion mode. Signals of the compound were monitored under the multiple reaction monitoring (MRM) for quantification. The brain microdialysates and the blood samples were collected simultaneously after intraperitoneal injection of the compound (50 mg.kg-1) during 12 hours from freely moving rats. Plasma samples were analyzed after simple two-step protein precipitation using with MeOH after sampling from rat and 10% perchloric acid before analysis, however clean-up for microdialysis samples was not necessary, enabling direct injection of the samples into the LC-MS/MS system.

RESULTS:

The precursor to product ion transition of m/z 256 > m/z 144.8 was used to measure concentrations of lamotrigine with a retention time of 5.4 min. The method was validated in both plasma and microdialysate samples and the obtained lower limit of quantification (LLOQ) was 0.1 ng.mL-1 for lamotrigine in both matrices. The intra- and inter- day assay variability was less than 15 % for both analytes.

CONCLUSIONS:

The proposed LC-MS/MS method provided simple sampling, rapid clean-up and short analysis time (<6 min), and is applicable to the routine therapeutic monitoring and pharmacokinetic studies of lamotrigine.

ACKNOWLEDGEMENTS:

This work was supported by the Scientific Research Projects Commission of Anadolu University (Project No 1301S009) and all animal experiments were performed in accordance with the principles of animal use and care approved by the ethical committee of the Medical Faculty of Osmangazi University (Approval File No. 04/2007)

P-195: AN ELECTROCHEMICAL SENSOR FOR SENSITIVE AND FAST DETECTION OF MITOXANTRONE BASED ON NANO-SEPIOLITE ELECTRODE

Eskikoy Bayraktepe, D., Yildiz, C., Yazan, Z.

Ankara University, Department of Chemistry, Ankara, Turkey

INTRODUCTION:

Mitoxantrone (MTX) is a significant antitumor drug against breast and prostate cancers, acute leukemia and non-Hodgkin's lymphoma (1, 2). The overdose of MTX in human can cause serious side effects such as fever, chills, sore throat, flu symptoms, easy bruising or bleeding (nosebleeds, bleeding gums), loss of appetite, mouth sores, unusual weakness etc. (3). Hence, it is very important to develop simple and reliable methods for fast and accurate detection of MTX. For his reason, in this study is to develop a new, sensitive and selective electrochemical method for determination of MTX in serum and pharmaceutical samples.

MATERIALS AND METHODS:

Mitoxantrone, graphite powder, mineral oil and sepiolite clay were purchased from Sigma Aldrich Company. 0.1 M H_2SO_4 solution was used for supporting electrolyte. Cyclic voltammetry (CV), Differential Puls Adsorptive Stripping Voltammetry (AdsDPV) and Electrochemical Impedance Spectroscopy (EIS) measurements were carried out by using CHI 760B (from USA) connected with electrochemical workstation and C3 cell stand (BASi).

A three-electrode system was used and nano-sepiolite clay modified carbon paste sensor (NSC/CPE) was used as working electrode, Ag/AgCl (BAS MW-1032) was used as reference electrode and platinum electrode was used as auxiliary electrode (BAS MF-2052).

RESULTS:

Firstly, sepiolite modified carbon paste sensor was prepared by adding appropriate amounts of sepiolite clay, graphite and mineral oil and then, newly designed surface of sensor was characterized by using SEM,

EIS and CV techniques. Secondly, AdsDPV method was developed to determine MTX in biological and pharmaceutical samples based on NSC/CPE sensor. The anodic peak current of MTX in AdsDPV varies linearly with the concentration range of 2.42 – 100 n mol L-1. Dedection (LOD) and quantification (LOQ) limits were calculated as 0.7261 n mol L-1 and 2.42 n mol L-1, respectively. The voltammetric technique was applied to MTX analysis in human serum and flacon samples. The results found satisfactorily.

CONCLUSIONS:

For the first time, sensitive, selective and reproducible electrochemical method was developed for the electro-analysis of MTX in pharmaceutical and human serum samples using NSC/CPE sensor.

ACKNOWLEDGEMENTS:

This study was supported by Ankara University Research Fund (Project Numbers: 13L4240009 and 15L0430006)

REFERENCES:

1. Tietze R, Schreiber E, Lyer S, Alexiou C (2010). Biomed. Res. Int, 1-8.
2. An G, Morris ME (2010). J. Pharm. Biomed. Anal, 51:750-753.
3. https://www.emedicinehealth.com/drug-mitoxantrone/article_em.htm#sideeffects

P-196: ELECTROCHEMICAL SENSOR FOR THE DETERMINATION OF ANTI-CANCER SHIKONIN BASED ON NSC/TIO2/MWCNTS COMPOSITE

Eskikoy Bayraktepe, D., Yazan, Z.

Ankara University, Department of Chemistry, Ankara, Turkey

INTRODUCTION:

A number of pharmaceutical studies have shown that Shikonin (SHI) has some antibacterial, antifungal, antimicrobial, anti-inflammatory and antithrombotic activity in humans (1). It has a cytotoxic effect on 15 different cancer cell lines, including some multidrug - resistant ones (2). For this reason, it is very important to develop simple and reliable methods for accurate detection of SHI. In this study, we aimed to develop a new sensor based on sepiolite clay, TiO2 nanoparticles and multiwall carbon nanotubes composite for sensitive determination of SHI in human urine and serum samples.

MATERIALS AND METHODS:

Shikonin, graphite powder, mineral oil and nano-sepiolite clay, multiwall carbon nanotubes (MWCNTs) were purchased from Sigma Aldrich Company. 0.1 M H2SO4 solution was used for supporting electrolyte. Cyclic voltammetry (CV), Square wave adsorptive stripping voltammetry (AdsSWV) and Electrochemical Impedance Spectroscopy (EIS) measurements were carried out by using CHI 760B (from USA) electrochemical workstation and C3 cell stand (BASi). Traditional three-electrode system was used and nano-sepiolite clay, TiO2 nanoparticles and MWCNTs modified carbon paste sensor (NSC/TiO2/MWCNTs/CPE) was used as working electrode, Ag/AgCl (BAS MW-1032) was used as reference electrode and platinum electrode was used as auxiliary electrode (BAS MF-2052).

RESULTS:

AdsSWV method was developed to determine SHI in biological samples based on NSC/TiO2/MWCNTs/CPE sensor. Firstly, the composite sensor (NSC/TiO2/MWCNTs/CPE) was prepared and the surface characterization of this sensor was carried out by using EIS, CV and SEM techniques. Secondly, based on anodic peak current of SHI in AdsSWV, the calibration study was done and linear concentration range varies linearly with the concentration range of 1.30 – 1000 nmol L-1. Detection (LOD) and quantification (LOQ) limits were calculated as 0.39 nmol L-1 and 1.30 nmol L-1, respectively. The voltammetric technique was applied to SHI analysis in human serum and urine samples. The recovery results are about 100%.

CONCLUSIONS:

A new, sensitive, selective and reproducible AdsSWV method was developed for the analysis of SHI in human serum and urine samples using NSC/TiO2/MWCNTs/CPE sensor.

ACKNOWLEDGEMENTS:

Ankara University Research Fund supported this study (Project Numbers: 13L4240009 and 15L0430006)

REFERENCES:

1. Huang YI, Cheng YH, Yu CC, Tsai TR, Cham TM (2007). Colloids and Surfaces B: Biointerfaces, 58:290–297.
2. Wiench B, Eichhorn T, Paulsen M, Efferth T (2012). Evidence-Based Complementary and Alternative Medicine, 1-15.

P-198: VOLTAMMETRIC AND SPECTROELECTROCHEMICAL BEHAVIOR OF NOVEL OCTA SUBSTITUTED METALLOPHTHALOCYANINES

Orman, EB., Huraibat, B., Atajanov, R., Odabas, Z., Ozkaya, AR.

Marmara University, Department of Chem., Istanbul, Turkey

INTRODUCTION:

Phthalocyanines owe their importance to the applications in various fields such as press ink dye and pigments, non-linear optics, photodynamic therapy (PDT), and semiconductors since their first synthesis early in the last century (1). Their classical use has been broadened in recent years by other areas of current interest including applications in electrocatalysis, electrochromism, energy producing systems as fuel cells, which are closely related to their unique electron transfer properties (2). Thus, the identification of electrochemical and in-situ spectroelectrochemical properties of the newly synthesized metallophthalocyanine (MPc) compounds has vital importance in terms of their technological applications. In recent years, some metallophthalocyanines, especially iron and cobalt Pcs have been used in catalytic reactions because of their rich and modifiable electrochemical and spectroelectrochemical properties resulting from metal-based redox activity (3).

In this study, the electrochemical and in-situ spectroelectrochemical characterization of the novel Co(II), Cu(II), Fe(II) and Mn(II) 2,3,9,10,16,17,23,24-octa(2-isopropyl-5-methylphenoxy)phthalocyanine complexes have been performed in non-aqueous solution.

MATERIALS AND METHODS:

Cyclic voltammetry (CV) and square wave voltammetry (SWV) techniques were used to identify electrochemical redox properties in solution medium.

RESULTS:

The compounds displayed both Pc ring- and/or central metal-based rich redox properties. Spectroelectrochemical measurements provided strong support for identification of their redox processes.

CONCLUSIONS:

Complex Cu(II) shows Pc ring-based one electron redox processes whereas Co(II), Fe(II) and Mn(II) complex produce both Pc ring and metal-based one electron redox processes.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Marmara University-BAPKO (Project No: FEN-C-YLP-200318-0114)

REFERENCES:

1. Wang H, Wang BW, Bian Y, Gao S, Jiang J (2016). Coordination Chemistry Reviews, 306:195-216.
2. Lever ABP, Milaeva ER, Speier G (1993). In Phthalocyanines: Properties and Applications; Eds.; VCH: New York, Vol. 3, pp 1–69.
3. Orman EB, Altun S, Odabas Z, Altindal A, Ozkaya AR (2015). Journal of The Electrochemical Society, 162(12): 825-840.

P-199: DEVELOPMENT OF AN ACCURATE AND SENSITIVE ANALYTICAL METHOD FOR THE DETERMINATION OF DIOSMIN BY USING HPLC

[1] Erk, N., [2] Sari, MT.,[1] Sahin, E.

[1]Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

[2]Drogsan Phar. Ind Ankara,Turkey

INTRODUCTION:

Diosmin (Dio) is a type of plant chemical found mainly in citrus fruits. Dio is a semisynthetic drug indicated for the treatment of venous disease. Diosmin is a flavone that can be found in the plant Teucrium gnaphalodes. Other name is 3',5,7-trihydroxy-4'-methoxyflavone-7-rhamnoglucoside, Bioflavonoid, Bioflavonoid Complex. In this study, rapid, simple and Sensitive reversed-phase liquid chromatographic determination was described for the assay of Dio in bulk and tablet formulations.

MATERIALS AND METHODS:

Optimal separation and determination of Dio was achieved with a Nucleosil 100 C18 125 x 4.6 mm, 5 µm analytical column using water :glacial acetic acid :methanol (61.5:4.5:34.0 v/v/v) as a mobile phase in isocratic mode with flow rate of 1.5 mL/min-1,loop of 10 µL.

RESULTS:

The maximum absorption wavelength of Dio is 275.0 nm was studied as the detection wavelength and column at 400C temperature. The retention time of Dio was observed at 5.88nm. Under optimized conditions, RP-HPLC method exhibited the wide linear working regions with the coefficient value r2 of > 0.9996, and the mean recovery value was 99.3 % .

CONCLUSIONS:

The present successfully validated method with selectivity, linearity, sensitivity, precision and accuracy was applicable for the assay of Dio in bulk drug substance an pharmaceutical dosage forms.

REFERENCES:

1. Ameer B et al., (1996). Clin. Pharmacol.Ther., 60: 34-40.
2. Pehivan M et al., (2004). Acta Chir Belg., 104(6):715-718.
3. Friesenecker B et. al., (1994) Int. J.Microcirc. Clin. Exp., 14: 50–55.

P-200: HIGH YIELD SYNTHESIS OF MOF FUNCTIONALIZED NANOPARTICLE FOR DETERMINATION OF HCG

[1,5]Ahi, EE., [1] Torul, H., [2] Zengin, A., [3] Suludere, Z., [4] Selbes, Y.,[5] Durmus, M.,[1] Tamer, U.

[1]Gazi University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

[2]Van Yüzüncü Yıl University, Faculty of Engineering and Architecture, Department of Chemistry Technologies, Van, Turkey

[3]Gazi University, Faculty of Science, Department of Biology, Ankara, Turkey

4Hacettepe University, Turkey Doping Control Center, Ankara, Turkey

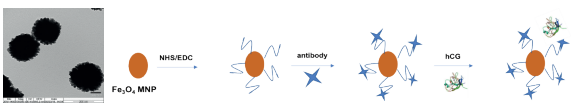
5Gebze Technical University, Faculty of Science, Department of Chemistry, Kocaeli, Turkey

INTRODUCTION:

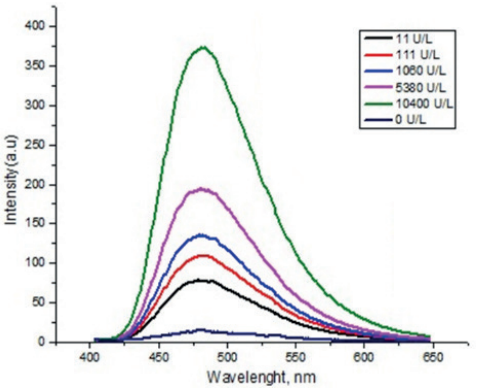
The use of human chroionic gonadotropin (hCG, a glycoprotein hormone) as a performance enhancing drug has been prohibited by the World Anti-Doping Agency (1). Determination of hCG in urine is used to detect illicit use of hCG. In this study, we demonstrated a fluorescamine based method which includes magnetic separation of hCG.

MATERIALS AND METHODS:

Magnetic nanoparticles were synthesized by solvothermal method and modified with mercaptoacetic (MAA) acid to induce MOF growth onto the nanoparticles. Fe3O4@MAA nanoparticles were dispersed in FeCl3.6H2O and then kept standing for 15 min. The obtained nanoparticles were collected by a magnet and washed with plenty of ethanol. Subsequently, the nanoparticles were dispersed in benzenetricarboxylic acid, kept stewing for half an hour at 70 °C, separated by a magnet and washed with ethanol. After repeating for 30 cycles, the synthesized nanoparticles were dried under vacuum at 200 °C.



The newly synthesized magnetic nanoparticles were conjugated with hCG antibodies using EDC/NHS activation approach. Then antibody conjugated MNPs were used to capture hCG molecules. The captured hCG molecules were taken into borate buffer (pH: 9.0). Finally, fluorescamine solution was added to form a fluorescent product with primary amines of proteins. Then the fluorescence intensity was measured to quantify the hCG molecules.



RESULTS AND CONCLUSIONS:

Analytical performance of the system was investigated by examining with different concentration of hCG. A linear response (0.9123) was obtained between fluorescence intensity and hCG concentration in the range of 11 U/L to 10400 U/L. The results indicate that the developed fluorometric method can be used in quantitative analysis of hCG samples.

REFERENCES:

1. Stenman UH, Hotakainen K, Alfthan H (2008). British Journal of Pharmacology, 154:569-583.

P-201: NEW SAMPLE PREPARATION METHOD FOR ANALYSIS OF POLAR AND NON-POLAR METABOLITES

Kocak, E., Kaplan, O., Celebier, M.

Hacettepe University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

The metabolome is the terminal downstream product of the genome and consists of the total complement of all the low molecular weight molecules (metabolites) in a cell, tissue or organism. Metabolomics aims to measure a wide breadth of small molecules in the context of physiological stimuli or in disease states (1). Metabolomics methodologies fall into two distinct groups; untargeted metabolomics, an intended comprehensive analysis of all the measurable analytes in a sample including chemical unknowns, and targeted metabolomics, the measurement of defined groups of chemically characterized and biochemically annotated metabolites. For untargeted metabolomics main goal is to reach maximum number of identified metabolites. New sample preparation methods, analytical techniques and bioinformatics have been developed for this purpose in recent years. In this study a new sample preparation method was used to separate polar and non-polar metabolites and it was proposed for further studies.

MATERIALS AND METHODS:

Metabolites were separated from other biomolecules like lipids and proteins by using extraction. Methanol/chloroform/water mixture was used for the extraction of polar and non-polar metabolites where ultrafiltration system was used for the purification of metabolites from lipids. Polar metabolites were dissolved in methanol/water phase and non-polar metabolites and lipids were dissolved in chloroform phase. Polar and non-polar metabolites were analyzed with LC/MS and MS data were evaluated by using XCMS data processing system.

RESULTS:

249 polar metabolite and 60 non-polar metabolite were identified with this method.

CONCLUSIONS:

New sample preparation method could be used for metabolite enrichment and in the futher this methodology could be used for clinic samples.

REFERENCES:

1. Bligh EG, Dyer WJ (1959). Can J Biochem Physiol, 37:911–917.

P-202: DETERMINATION OF FATTY ACID SYNTHASE PROTEIN IN MCF-7 CANCER CELLS BY USING UPLC/MS METHOD

[1] Kocak, E., [1] Kaplan, O., [1] Celebier, M., [2] Ercan, A.

[1]Hacettepe University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

[2]Hacettepe University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey

INTRODUCTION:

Fatty acid synthase (FASN), which catalyzes the synthesis of long-chain fatty acids, is a key protein for cell structure. Especially, FASN is very important for lipid formation and energy production in cancer cells. Therefore FASN expression level is important on tumor development (1). In recent years, the studies showed that FASN expression level in cancer cells was higher than normal cells. FASN has been become cancer marker and therapeutic target for cancer treatment. FASN inhibitors have been evaluated as new anticancer agents for treatment of many cancer types. Therefore, determination of FASN expression is crucial for monitoring of cancer development and developing of new alternative cancer treatment methods. In this study UPLC/MS method was evaluated to determine FASN in MCF-7 breast cancer cells.

MATERIALS AND METHODS:

Proteins of MCF-7 cells, which were isolated with methanol/chloroform/water mixture, digested with trypsin enzyme. Peptide mixtures were separated in C18 UPLC column (2,1x100mm, 1,8µm). Flow rate was adjusted at 0,2 mL/min. A gradient elution program was performed for 150 minutes. Water and acetonitrile were used as mobile phases. Peptides were analyzed with Q-TOF-MS system and recorded MS-MS data were matched with in silico data to identify peptides and FASN. Label free quantification algorithm was also used to observe whether UPLC system was suitable for semi quantitative analysis of FASN. Protein identification and quantification were processed with Maxquant proteomics software.

RESULTS:

12 peptides belonging to FASN were identified with three replicates. Identified peptides showed %10,9 coverage of FASN. Method reproducibility and robustness were evaluated with peptide retention times, matching scores, peptide intensity and protein intensity.

CONCLUSIONS:

Easy, robust and reproducible UPLC/MS system offered new approach to determine the cancer marker and therapeutic target FASN. In the future, UPLC/MS method could be used for FASN determination in tissue and body fluid samples.

REFERENCES:

1. Menendez JA, Lupu R (2007). Nat Rev Cancer, 7(10):763-777.

P-203: PLS AND PCR CALIBRATION MODELS FOR SPECTRAL ANALYSIS OF ATORVASTATIN AND EZETIMIBE

Dinc, E., Ertekin, ZC.

Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

The combination of atorvastatin (AT) and ezetimibe (EZ) is mainly used for the treatment of elevated LDL-cholesterol levels (1). In this study, we aim to develop fast and reliable spectrophotometric analysis for the concurrent analysis of AT and EZ in tablets.

MATERIALS AND METHODS:

Standard solutions of AT and EZ were prepared between of 4.0-36.0 µg/mL. Absorbance spectra of the solutions were recorded between 200-350 nm. Classical least squares was unable to quantify AT and EZ in their combination due to their overlapping spectra. Partial least squares (PLS) and principle component regression (PCR) calibrations were constructed using the actual concentration values and absorbance data (2). As can be seen in Figure 1, the number of components were found as 2 for both drugs in both models.

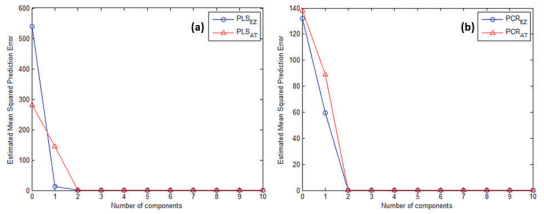


Figure 1. Estimated mean squared prediction error values for (a) PLS and (b) PCR models

The coefficients of the regression between the actual and predicted concentrations of PLS and PCR models were reported to be greater than 0.99991 for both drugs. The proposed methods were validated by analyzing synthetic binary mixtures, intra-day and inter-day samples, and standard addition samples. Then, they applied to the analysis of commercial samples containing 10 mg EZ and 10 mg AT per tablet.

RESULTS:

The validation studies were found to be satisfactory for both PLS and PCR models. The proposed methods were successfully applied to the analysis of tablets.

CONCLUSIONS:

The proposed PLS and PCR calibration models were suitable for the quality control and routine analysis of tablets containing AT and EZ without the use of a preliminary separation step.

REFERENCES:

1. Lee et al., (2012). Journal of Cardiovascular Pharmacology and Therapeutics, 17:65-71.
2. Dinç et al., (2008). Journal of Pharmaceutical and Biomedical Analysis, 48:471-1475.

P-204: SIMULTANEOUS DETERMINATION OF ATENOLOL AND CHLORTHALIDONE IN TABLETS BY PLS AND PCR METHODS

Dinc, E., Ertekin, ZC.

Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

The combination of atenolol (ATE) and chlorthalidone (CHL) is commonly used for the treatment of hypertension. The purpose of this study was to develop a simple and low-cost analysis method for the concurrent analysis of ATE and CHL in a tablet formulation.

MATERIALS AND METHODS:

A classical spectrophotometric calibration curve for ATE and CHL was not possible to obtain because of the overlapping spectra of the mentioned drug. In this study, we used two standard chemometric techniques, partial least squares (PLS) and principle component regression (PCR) in order to quantify ATE and CHL in their mixtures (1).

A calibration set of 25 binary mixtures containing ATE and CHL in the working range of 6-30 µg/mL and 4-16 µg/mL was prepared and their UV absorbance spectra were recorded between 200-3 nm. PLS and PCR algorithms were applied to nominal concentration and absorbance data of the concentration set. Recovery studies were performed by analyzing 12 laboratory-made mixtures of ATE and CHL, using the constructed calibration equations. Standard addition, inter-day and intra-day studies were also performed in order to evaluate the validity of the methods.

RESULTS:

The proposed PLS and PCR methods were applied to the analysis of pharmaceutical preparations containing 100 mg ATE and 25 mg CHL per tablet. The assay results of PLS were reported as 99.41 mg and 25.60 mg, and PCR results were reported as 99.61 mg and 25.66 mg per tablet for ATE and CHL, respectively.

CONCLUSIONS:

PLS and PCR methods proposed in this study were successfully used for the simultaneous determination of ATE and CHL in tablets without the need of any separation step.

REFERENCES:

1. Dinc et al., (2008). Journal of Pharmaceutical and Biomedical Analysis, 48:471-1475.

P-205: LC-MS/MS METHOD FOR THE DETERMINATION OF OXCARBAZEPINE IN RAT PLASMA AND BRAIN MICRODIALYSATE

[1] Sener, E., [1] Dogrukol Ak, D., [2] Korkmaz, OT.

[1]Anadolu University, Faculty of Pharmacy, Department of Analytical Chemistry, Eskişehir, Turkey

[2]Osmangazi University, Faculty of Medicine, Department of Physiology, Eskişehir, Turkey

INTRODUCTION:

A fast, specific and highly sensitive liquid chromatography tandem mass spectrometry (LCMS/MS) method for the direct determination of oxcarbazepine which is an anti-epileptic compound in rat plasma and brain microdialysate has been developed and validated.

MATERIALS AND METHODS:

The analysis was performed on a Supelco Ascentis Express C18 (100x2.1 mm, 2.7 µm particle) core shell column using a binary gradient elution with the mobile phases consisting of acetonitrile and ammonium formate buffer (10 mM). Ionization of the compound was achieved by electrospray ionization (ESI) in

positive ion mode. Signals of the compound were monitored under the multiple reaction monitoring (MRM) for quantification. The brain microdialysates and the blood samples were collected simultaneously after intraperitoneal injection of the compound (50 mg.kg-1) during 12 hours from freely moving rats. Plasma samples were analyzed after simple two-step protein precipitation using with MeOH after sampling from rat and 10% perchloric acid before analysis, however clean-up for microdialysis samples was not necessary, enabling direct injection of the samples into the LC-MS/MS system.

RESULTS:

The precursor to product ion transition of m/z 253 > m/z 179.8 was used to measure concentrations of oxcarbazepine with a retention time of 6.2 min. The method was validated in both plasma and microdialysate samples and the obtained lower limit of quantification (LLOQ) was 0.1 ng.mL-1 for oxcarbazepine in both matrices. The intra- and inter-day assay variability was less than 15 % for both analytes.

CONCLUSIONS:

The proposed LC-MS/MS method provided simple sampling, rapid clean-up and short analysis time (<6.5 min), and is applicable to the routine therapeutic monitoring and pharmacokinetic studies of oxcarbazepine.

ACKNOWLEDGEMENTS:

This work was supported by the Scientific Research Projects Commission of Anadolu University (Project No 1301S009). All animal experiments were performed in accordance with the principles of animal use and care approved by the ethical committee of the Medical Faculty of Osmangazi University (Approval File No. 04/2007)

P- 206: LC-MS/MS METHOD FOR THE DETERMINATION OF TOPIRAMATE IN RAT PLASMA AND BRAIN MICRODIALYSATE

[1] Sener, E., [1] Dogrukol Ak, D., [2] Korkmaz, OT.

[1]Anadolu University, Faculty of Pharmacy, Department of Analytical Chemistry, Eskisehir, Turkey

[2]Osmangazi University, Faculty of Medicine, Department of Physiology, Eskisehir, Turkey

INTRODUCTION:

A fast, specific and highly sensitive liquid chromatography tandem mass spectrometry (LC-MS/MS) method for the direct determination of topiramate which is a polar anti-epileptic compound in rat plasma and brain microdialysate has been developed and validated.

MATERIALS AND METHODS:

The analysis was performed on a Supelco Ascentis Express C18 (100x2.1 mm, 2.7 µm particle) core shell column using a binary gradient elution with the mobile phases consisting of acetonitrile and ammonium formate buffer (10 mM). Ionization of the compound was achieved by electrospray ionization (ESI) in negative ion mode. Signals of the compound were monitored under the multiple reaction monitoring (MRM) for quantification. The brain microdialysates and the blood samples were collected simultaneously after intraperitoneal injection of the compound (50 mg.kg-1) during 12 hours from freely moving rats. Plasma samples were analyzed after simple two-step protein precipitation using with MeOH after sampling from rat and 10% perchloric acid before analysis, however clean-up for microdialysis samples was not necessary, enabling direct injection of the samples into the LC-MS/MS system.

RESULTS:

The precursor to product ion transition of m/z 388 > m/z 77.6 was used to measure concentrations of topiramate with a retention time of 6.4 min. The method was validated in both plasma and microdialysate samples and the obtained lower limit of quantification (LLOQ) was 2.0 ng.mL-1 for topiramate in both matrices. The intra- and inter-day assay variabilities were less than 15 % for both analytes.

CONCLUSIONS:

The proposed LC-MS/MS method provided simple sampling, rapid clean-up and short analysis time (<7 min), and is applicable to the routine therapeutic monitoring and pharmacokinetic studies of topiramate.

ACKNOWLEDGEMENTS:

This work was supported by the Scientific Research Projects Commission of Anadolu University (Project No 1301S009) and all animal experiments were performed in accordance with the principles of animal use and care approved by the ethical committee of the Medical Faculty of Osmangazi University (Approval File No. 04/2007)

P-207: ELECTROCHEMICAL DETECTION OF ISOQUINOLINES IN HUMAN SERUM AND URINE SAMPLES

[1,4] Kivrak, E., [2] Bozkurt, B., [3] Durmaz Armagan, G., [1,4] Yuksel, S. [2] Unver Somer, N., [1] Kara, P.

[1]Ege University, Faculty of Pharmacy, Department of Analytical Chemistry, Izmir, Turkey

[2]Ege University, Faculty of Pharmacy, Department of Pharmacognosy, Izmir, Turkey

[3]Ege University, Faculty of Pharmacy, Department of Biochemistry, Izmir, Turkey

4Ege University, Faculty of Engineering, Department of Biomedical Techniques , Izmir, Turkey

INTRODUCTION:

Isoquinolines, the largest group of alkaloids, have been found to exhibit interesting pharmacological and/or biological properties. Berberine, stylopine, isocorydine and glaucine, the isoquinoline alkaloids distributed in some genus of Papaveraceae, Magnoliaceae, Rutaceae, Ranunculaceae, Annonaceae, Berberidaceae, Menispermaceae are extensively investigated due to their therapeutic actions (1). Berberine is one of the most studied among the protoberberine alkaloids with multiple biological activities such as antiinflammatory, antiplatelet, antimicrobial, cytotoxic, vasorelexant and hypotensive effect (2). Stylopine, isocorydine and glaucine are major component of various medicinal plants, they have been reported to important pharmacological effects including anti-inflammatory, antipsychotic, neuroleptic, sedative, antitussive and anticancer activity.

Due to their bioactivity and wide potential applications, a number of analytical methods including liquid and gas chromatography, mass spectrometry, fluorescence have been reported for the determination of these alkoloids (3). Although chromatographic methods are sensitive and reliable, they have some disadvantages such as being time and labor consuming, expensive, require sample pretreatment and qualified personnel. Electroanalytical methods, which can offer high sensitivity, rapid response, easy operation and low cost detection.

MATERIALS AND METHODS:

MWCNT's were modified with pencil graphite electrode surfaces. SWV voltammetry was used for detect the electrochemical behaviours of berberine, isocorydine, protopine and glaucine. These alkaloids were spiked into human serum and urine samples. And SWV responses were evalutaed before and after spiked.

RESULTS:

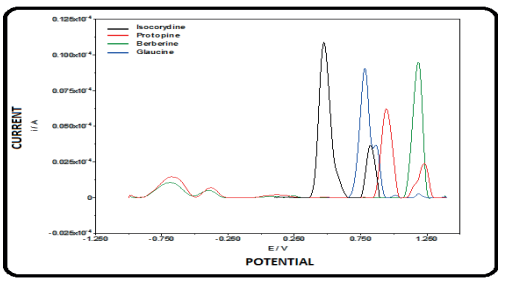


Figure: SWV voltammograms obtained from, berberine, isocorydine, protopine and glaucine at MWCNT/PGE surfaces.

CONCLUSIONS:

In this study, MWCNTs enhanced graphite sensor surfaces were used for direct electrochemical detection of isoquinoline alkoloids including berberine, isocorydine, protopine and glaucine for the first time. Investigation of electrochemical behaviours of these alkoloids in human serum and urine samples were also evaluated devoted to pharmaceutical applications.

REFERENCES:

1. Altan VM, Arioglu E, Guner S, Ozcelikay AT (2007). Heart Failure Reviews, 12:58-65.
2. Correia MA (2012). In: Katzung BG (ed). Basic and Clinical Pharmacology. Mc Graw Hill Education, United States of America, pp 56-73.
3. Geto A et al., (2013). Sensors and Actuators B: Chemical, 183: 96-101.

P- 208: VOLTAMMETRIC DETERMINATION OF EPHEDRINE ON POLY (NILE BLUE) MODIFIED GLASSY CARBON ELECTRODE IN PHARMACEUTICAL DOSAGE FORMS AND URINE SAMPLES

Agin, F., Ozturk, G., Kul, D.

Karadeniz Technical University, Faculty of Pharmacy, Department of Analytical Chemistry, Trabzon, Turkey

INTRODUCTION:

Ephedrine, is a naturally occurring sympathomimetic drug derived from the botanical plant Ephedra. Its principal mechanism of action relies on its indirect action on the adrenergic receptor system. Ephedrine was used as a drug in the treatment of asthma, allergic states, catalepsy and myasthenia gravis; to raise the arterial pressure; as nasal decongestive; as an antidote for poisoning by central nervous system depressants and in spinal anesthesia. Ephedrine was included in the doping list published by the International Olympic Committee (1). Therefore, monitoring ephedrine levels is a very important in both urine samples and pharmaceutical formulations. For this reason, the modified electrode was prepared for voltammetric determination of ephedrine.

MATERIALS AND METHODS:

A three-electrode electrochemical cell was used for the experiments. It contained a (BAS, ϕ: 3 mm diameter) as working electrode, a platinum wire as counter electrode and Ag/AgCl electrode as reference. All measurements by cyclic voltammetry and differential pulse voltammetry were performed using a computer-controlled Autolab potentiostat/galvanostat with Nova 10.0 software (Metrohm-Autolab, The Netherlands).

RESULTS:

The modified electrode was prepared electropolymerisation of monomer Nile blue (NB). The electropolymerisation of monomer NB on the surface of the GCE was carried out in 0.1 M phosphate buffer solution, at pH 6.0 containing 0.5 mM NB monomer by cyclic voltammetry (2). The electrochemical behavior of ephedrine was investigated using cyclic and differential voltammetry poly(NB) modified glassy

carbon electrode at different pH values between 5.0-9.0. A diffusion-controlled irreversible oxidation peak was observed in cyclic voltammetry for ephedrine. Quantitative determination of ephedrine was carried out at poly(NB) modified glassy carbon electrode using differential pulse voltammetry in 0.04 M Britton-Robinson buffer at pH 9.0. The peak current showed a linear dependence with concentration in the range of 0.6-100 µM with 0.00291 µM limit of detection for differential pulse voltammetry.

CONCLUSIONS:

Simple, selective, sensitive, fully validated, rapid, reliable, differential pulse voltammetry and poly(NB) modified glassy carbon electrode was used for the voltammetric determination of ephedrine in human urine and pharmaceutical formulations. No electroactive interferences from the pharmaceutical dosage forms excipients were found.

REFERENCES:

1. Mersal GAM (2012). J Solid State Electrochem., 16:2031-2039.
2. Kul D, Pauliukaite R, Brett CMA (2011). Journal of Electroanalytical Chemistry, 662:328-333.

P-209: ELECTROANALYTICAL DETERMINATION OF NIMESULIDE USING MULTIWALLED CARBON NANOTUBES MODIFIED CARBON PASTE ELECTRODE

Agin, F., Serdaroglu, V.

Karadeniz Technical University, Faculty of Pharmacy, Department of Analytical Chemistry, Trabzon, Turkey

INTRODUCTION:

Nimesulide is a new non-steroidal anti-inflammatory drug that is selective for cyclooxygenase-2 and effective in reducing the pain which is associated with rheumatoid arthritis and osteoarthritis (1).

Applications of carbon nanotubes as electrode materials or modifiers of conventional working electrodes in analytical chemistry can be found in the literature, because of a lower over potential and higher peak currents are observed in the voltammetric response at electrodes modified (2). In this study, a sensitive multiwalled carbon nanotubes modified carbon paste electrode was prepared for electroanalytical determination and it used to investigate electro-oxidative behavior of nimesulide with cyclic and differential pulse voltammetry.

MATERIALS AND METHODS:

A three-electrode electrochemical cell was used for the experiments. It contained a carbon paste electrode (BAS, ϕ: 3 mm diameter) as working electrode, a platinium wire as counter electrode and Ag/AgCl electrode as reference. All measurements by cyclic voltammetry and differential pulse voltammetry were performed using a computer-controlled Autolab potentiostat/galvanostat with Nova 10.0 software (Metrohm-Autolab, The Netherlands).

RESULTS:

The voltammetric behavior and determination of nimesulide was investigated by cyclic voltammetry and differential pulse voltammetry on multiwalled carbon nanotubes modified carbon paste electrode in various buffer solutions at different pH values between 2.0 and 8.0. The oxidation process of nimesulide exhibited irreversible and diffusion-controlled behavior in cyclic voltammetry. The best peak shape with peak current of nimesulide for quantitative determination were obtained in 0.1 M phosphate buffer solution at pH 5.0. The multiwalled carbon nanotubes modified carbon paste electrode showed linearity in the range from 0.06 and 10 µM of nimesulide with limit of detection 1.07×10-3 µM and limit of quantification 3.24×10-3 µM by differential pulse voltammetry.

CONCLUSIONS:

Carbon paste electrode was modified with multiwalled carbon nanotubes and optimized for nimesulide. The prepared modified carbon paste electrode was used electroanalytical determination of nimesulide cyclic voltammetry and differential pulse voltammetry. The multiwalled carbon nanotubes modified carbon paste electrode for electroanalytical determination of nimesulide using differential pulse voltammetry was carried out highly selectively, simply and stably from pharmaceutical dosage forms and human serum samples.

REFERENCES:

1. Quattrini M, Paladin SA (1995). Clin Drug Invest, 10:39-146.
2. Rivas GA et. al., (2007). Talanta, 74:291-307.

P-212: QUANTITATIVE ANALYSIS OF AMLODIPINE AND ATORVASTATIN BY USING CONSTANT CENTER SPECTROPHOTOMETRIC TECHNIQUE

[1,2] Lotfy, HM., [3] Erk, N. , [4] Tiris, G., [3] Sahin, E.

[1]Cairo University, Faculty of Pharmacy, Analytical Chemistry Department, Cairo, Egypt

[2]Future University Faculty of Pharmaceutical Science and Pharmaceutical

Industries, Pharmaceutical Chemistry Department, Cairo, Egypt

[3]Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

4Bezmialem Vakif University, Faculty of Pharmacy, Department of Analytical Chemistry, Istanbul, Turkey

INTRODUCTION:

Hypertension is a complex disease, with numerous cardiovascular complications. The combination of amlodipine (AML) and atorvastatin (ATR) are used hypertension and dyslipidemia. Up to now, there is no official method for the determination of binary mixture of AML and ATR in any national pharmacopoeia. Novel spectrophotometric techniques were presented as useful alternatives for determination of AML and ATR in their binary mixtures.

METHODS:

The absorption spectra of AML and ATR show highly overlapped spectra. The constant center spectrophotometric technique was applied for the determination of AML and ATR without any pre-separation process. first derivative spectra ratio spectrophotometry is used solutions of standard and samples in methanol.

RESULTS:

The amplitudes 236.17 , 275.0 , 284.0 and 310.0 nm wavelengths were selected to determine of AML and ATR in binary mixture, respectively by the constant center spectrophotometric technique. The determination of AML, and ATR in (AML+ATR) binary mixtures could be done using the following equations : y= 0.9105 x- 0.4177 (r2 : 0.9999) for ATR ; and y=0.09243 x-0.0401 (r2 : 0.9999) for AML, respectively. The drugs obey Beer's Lambert law in the linear ranges are 5.0-35.0 ug/mL and 3.0-30.0 ug/mL for AML and ATR, respectively. The results of the assay were found to be 99.96 ± 0.96 for AML and 100.48 ± 1.14 for ATR.

CONCLUSION:

This validated technique is potentially useful for a routine laboratory analysis.The presented method was found to be simple, precise and accurate which can be directly and easily applied to the determination of pharmaceutical dosage forms.

P-213: VOLTAMMETRIC DETERMINATION OF CETIRIZINE IN PHARMACEUTICALS BY DIFFERENTIAL PULSE AND SQUARE WAVE VOLTAMMETRIC METHODS

Sofu, U., Ifsat, ZD., Ozturk, G., Kul, D.

Karadeniz Technical University, Faculty of Pharmacy, Department of Analytical Chemistry, Trabzon, Turkey

INTRODUCTION:

Cetirizine, (±)-[2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]acetic acid dihydrochloride, is one of the first second-generation H1 antihistamines developed to provide selective H1 receptor inhibition without central nervous system depression (1, 2). It is used for the symptomatic treatment of allergic conditions including allergic rhinites, chronic urticaria, and another allergic disorders (3). The aim of this work is to establish a method for the determination of cetirizine using modified glassy carbon electrodes.

MATERIALS AND METHODS:

All electrochemical experiments were performed with a three-electrode system including modified glassy carbon electrode as a working electrode, an Ag/AgCl as reference electrode and a platinum wire as counter electrode. Stock solutions of cetirizine (1x10-3 M) were prepared with doubly-distilled water. Phosphate buffer, Britton Robinson buffer and acetate buffer solutions at different pH values were prepared.

RESULTS:

Voltammetric methods were used for the determination of cetirizine in pharmaceuticals. For this purpose, modified glassy carbon electrodes were prepared according to the previous report (4). The effect of supporting electrolyte and voltammetric parameters were investigated. The optimum conditions were obtained in acetate buffer at pH 4.5. A well-defined peak was observed for cetirizine at about 0.9 V for both voltammetric methods. The linear response ranges for the determination of cetirizine were 0.4-100 µM and 0.2-100 µM with the detection limits of 2.70 nM and 5.80 nM for differential pulse and square wave voltammetry, respectively. The proposed methods were used to determine the cetirizine content of commercial tablets and satisfactory results were obtained.

CONCLUSIONS:

We have described sensitive, simple, rapid and selective voltammetric methods for the analysis of cetirizine in its pharmaceutical formulation.

REFERENCES:

1. Zhang L, Cheng L, Hong J (2013). Pharmacology, 92:14-25.
2. Likar MD, Mansour HL, Harwood JW (2005). Journal of Pharmaceutical and Biomedical Analysis, 39:543-551.
3. Rizk NMH, Abbas SS, EL-Sayed FA, Abo-Bakr A (2009). International Journal of Electrochemical Science, 4:396-406.
4. Yang G, Yan J, Qi F, Sun C (2010). Electroanalysis, 22:2729-2738.

P-214: ELECTROCHEMICAL MIP SENSOR FOR DETECTION OF BUTYRYLCHOLINE ESTERASE

[1] Ozcelikay, G., [2] Yarman, A., [1] Kurbanoglu, S., [1] Ozkan, SA., [3] Wollenberger, U., [3] Scheller, FW.

[1]Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

[2]Turkish-German University, Faculty of Science, Molecular Biotechnology, Istanbul, Turkey

[3]University of Potsdam, Institute of Biochemistry and Biology, Potsdam, Germany

INTRODUCTION:

Specific molecular recognition is a key feature of biological processes. In order to substitute biomacromolecules by "biomimetic recognition elements", fully synthetic receptors so-called molecularly imprinted polymers (MIPs) have been developed. Molecular imprinting is a method, pioneered by Wulff and Mosbach to create so-called plastic antibodies or plastibodies by the polymerization of functional monomers with or without cross-linkers in the presence of target analyte (template)(1,2). Subsequent removal of the template leads to the formation of binding cavities, which mimics size, shape, and functionality of the template. Although MIPs for low molecular-weight substances have been successfully prepared, it is still challenging for biomacromolecules like proteins. This is reflected by the annual number of publications for protein-MIPs, which is only 10 % including enzymes. The aim of the work is to prepare MIP-based sensors for the diagnostically relevant Butyrylcholine esterase (BuChE).

MATERIALS AND METHODS:

The o-phenylenediamine (o-PD) films were prepared by the electropolymerization of the o-PD monomer in the absence or in the presence of a BuChE Template molecules were removed by incubation in NaOH. All the steps of the MIP preparation were characterized by cyclic voltammetry and amperometry.

RESULTS:

The anodic current for the oxidation of thiocholine, which reflects the activity of the BuChE bound to the MIP increased almost linearly in the picomolar concentration range and did not approach saturation up to 2 nM. In the semilogarithmic plot saturation seems to be reached at 2 nM. On the other hand, for the MIP the signal were almost identical after electropolymerization, template removal and rebinding.

CONCLUSIONS:

A new electrochemical sensor based on a molecularly imprinted polymer has been developed for the detection of BuChE based on electropolymerization.

REFERENCES:

1. Wulff G (1984). New York Acad Sciences, 434: 327–333.
2. Mosbach K (1994). Trends In Biochemical Sciences, 19(1): 9-14.

P-215: ELECTROCHEMICAL INVESTIGATION OF ENTACAPONE USING NH2 FUNCTIONALIZED MULTI WALLED CARBON NANOTUBES MODIFIED NANOSENSOR

[1,2] Aftab, S., [1] Ozcelikay, G., [1] Kurbanoglu, S. [1,2] Shah, A., [1] Ozkan, SA.

[1]Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

[2]Quaid-i-Azam University, Department of Chemistry, Islamabad, Pakistan

INTRODUCTION:

Entacapone (ENP), is a selective, reversible catechol-O-methyl transferase inhibitor for the treatment of Parkinson's disease. It is a member of the class of nitrocatechols. When administered concomitantly with levodopa and a decarboxylase inhibitor (e.g., carbidopa), increased and more sustained plasma levodopa concentrations are reached as compared to the administration of levodopa and a decarboxylase inhibitor. Nanomaterials such as carbon based nanomaterials; (graphene, fullerene, carbon nanotubes, carbon nanofibers etc.), metal oxide nanoparticles, metal nanoparticles (gold, silver, platinum etc.), play important role in electrochemical determination of many drugs (1). In this study, electrochemical investigation of Entacapone using NH2 functionalized multi walled carbon nanotubes (NH2MWCNT) modified nanosensor was achieved.

MATERIALS AND METHODS:

NH2MWCNT (1mg/mL) suspension was prepared in dimethylformamide. A stock solution of 1.0×10−3 ENP was prepared with methanol. 20% (v/v) methanol percent was kept as constant in all pH values and buffers to avoid the solubility problems. Different amount of 1mg/mL NH2MWCNT was carefully dropped on the surface of pre-cleaned glassy carbon electrode (GCE). Then modified GCE was allowed to dry in vacuum oven at temperature of 45 ° C. NH2MWCNT/GCE electrode was thus obtained.

RESULTS:

NH2MWCNT was used as a recognition layer over the surface of GCE for the sensitive electroanalytical detection of antiparkinson drug Entacapone. The conditions were optimized for the getting intense electrochemical signals of the ENP. Surface morphology of the NH2MWCNT/GCE is assessed by SEM armed with EDX analysis. Analysis was made while imaging at different parts and at different resolutions. Electrochemical impedance spectroscopy (EIS) was used to investigate the electron transfer

capability of modified and bare electrodes with reference to 5.0 mM [Fe(CN)6]3-/4- and 0.1 M KCl redox couple system. Interfacial electron resistance can be changed during the electrode modification process. Cyclic voltammetry technique was successfully used to compare the redox response of ENP on the surface of modified and unmodified electrode. The electrochemical response of ENP was studied in 0.5M H2SO4 for modified and unmodified GCE with scan rate of 100mV/s. ENP shows an oxidation peak around 0.693 V and a reduction peak around 0.369 V for both electrodes.

CONCLUSIONS:

Generally, the electrocatalytic property of any catalytic material is judged by the electrochemical response, and if it facilitates an electron transfer process then the peak current. In this study, electrochemical investigation of Entacapone using NH2MWCNT/GCE is achieved. The influence of interfering agents was also studied to examine the selectivity of designed sensors because selectivity is one of the most important point to judge the reliability of a sensor for practical applications. For the purpose of the practical applicability of the proposed method, DPV method was effectively applied for the investigation of ENP in tablet, human serum and urine. Recoveries obtained for tablet, serum and urine samples were acceptable with RSD values less than 2% for all the samples with excellent recovery percentage close to 100%, thus, suggesting that NH2MWCNT/GCE has promising applicability and would be useful electrochemical sensor for quantitative analysis of ENP in pharmaceutical dosage and real samples.

REFERENCES:

1. Wang J (2005). Analyst, 130:421–426.

P-216: NOVEL "TURN OFF-ON" SENSORS FOR DETECTION OF DNA-ACRYLAMIDE INTERACTION USING ZNS QUANTUM DOTS AS A PHOSPHORESCENT PROBE

Satana Kara, HE.

Gazi University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

A novel "Turn off-on" sensor for detection of interaction between deoxyribonucleic acid (DNA) and Acrylamide (ACR) was developed.

MATERIALS AND METHODS:

In this method L-cysteine capped Mn doped ZnS quantum dots (QDs) were used as a room temperature phosphorescent probe. At the turn-off mode, ACR absorbed into the surface of QDs via electrostatic interaction which caused quenching effect of RTP signal by photo induced electron-transfer (PIET) mechanism. However, ACR removed from the QDs surface with the addition of DNA. Thus, the phosphorescence emission of QDs was recovered and the system consequently was rendered into "turn-on" mode.

RESULTS:

The quenching mechanism of QDs by ACR was collisional (dynamic) and quenching constant, binding constant, and binding site number were calculated as 3.2 × 104 M-1, 2.04 × 104 M-1, and 1.2, respectively. Besides, absorption spectrometric method was used to evaluate ACR-DNA interaction and binding constant (K) was found as 2.4 × 105 M-1.

CONCLUSIONS:

The developed this kind of biosensor is simple, free from the interferences coming from autofluorescence and scattering light, does not need any derivatization step and sample pretreatment. Thus, this biosensor can be used for the DNA analysis in the biological samples.

P-217: INVESTIGATION OF CHROMATOGRAPHIC BEHAVIOUR OF CLASS III ANTIARRHYTHMIC AGENT IN ACETONITRILE-WATER BINARY MIXTURES

Konce, I., Ortak, H., Daldal, YD., Nane, ID., Cubuk Demiralay, E., Alsancak, G.

Süleyman Demirel University, Faculty of Science and Literature, Department of Chemistry, [3]2260 Isparta, Turkey

INTRODUCTION:

Dofetilide is a sulfonamide class III antiarrhythmic agent and potassium channel blocker (Figure 1). Unlike other antiarrhythmic agents, oral dofetilide did not increase mortality in patients with a recent myocardial infarction or congestive heart failure. The available literature was scanned thoroughly, there was no reported methods for chromatographic behavior of dofetilide. In this study, method was preferred to investigate the retention behavior of dofetilide. The influence of eluent pH on the retention behavior of dofetilide was explored and the pKa values of this compound were determined. On the other hand, this study investigates on use of different percentages of acetonitrile-water binary mixtures and extrapolation to 100% water.

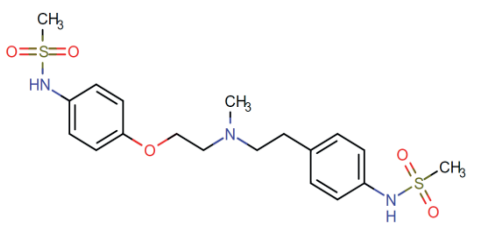


Figure 1. Structure of dofetilide

MATERIALS AND METHODS:

This study was performed at biorelevant temperature (37 0C) with Kinetex Core-Shell EVO C18 (5 µm, 250×4.6 mm) column. In this study, mobile phases used were different proportions of acetonitrile ranging from 20 to 30% (v/v). The pH of the mobile phase containing 30 mM o-phosphoric acid was adjusted by adding 1 M sodium hydroxide.

RESULTS:

The pKa values together with the tRHA and tRA from tR/pH data were calculated by using the nonlinear least squares fitting. The logtRHA is the retention time of the neutral form of the solute. The logtR values at different mobile phase sspH were calculated by considering the ionization of the solute. Based on the initial estimate, the predicted logtR was computed again and the best fit was obtained by minimizing the sum of squares of residual. The results show that better fit is clearly obtained by using nonlinear least squares curve fitting approach.

CONCLUSIONS:

This work represents the first study dealing with the chromatographic determination of pKa values of dofetilide at different proportions of acetonitrile-water binary mixtures.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (116Z837).

P-218: OPTIMIZATION AND VALIDATION OF VALPROIC ACID BY REVERSED PHASE LIQUID CHROMATOGRAPHY METHOD

Cengiz, A., Nane, ID., Ustun, Z., Konce, I., Ortak, H., Alsancak, G., Cubuk Demiralay, E.

Süleyman Demirel University, Faculty of Science and Literature, Department of Chemistry, Isparta, Turkey

INTRODUCTION:

Valproic acid (2-propylpentanoic acid) is a simple eight carbon branched-chain fatty acid with unique anticonvulsant properties against several types of epileptic seizures. Due to the widespread use of Valproic acid as an antiepileptic drug, there is no specific methods for the determination of this drug. In this study, simple, efficient and selective reversed phase liquid chromatography (RPLC) method has been developed for the determination of Valproic acid in tablet formulation. The aim of this study was to identify the optimum separation condition and the retention factor for Valproic acid based on a relationship between mobile phase pH and retention factors (1<k<10).

MATERIALS AND METHODS:

Column used was with flow rate of 1 mL min-1using UV visible detector for Valproic acid at 215 nm. The UV detector was operated at 210 nm for Oxacillin as internal standard. Experiments were performed with a commercially available column (Restek Pinnacle DB cyano, 250 x4,6 mm,5µm). All procedures were carried out at 298 K.

RESULTS:

The variation of retention factors at different pH values of the mobile phase is presented in Figure 1. The inflexion points of the curve specify the pKa value.

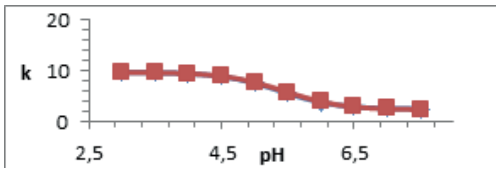


Figure 1. Dependence of retention factor values of Valproic acid on the pH of the mobile phase (20%MeOH v/v).

The described method was linear over a concentration range of 200-600 µgmL-1 for the assay of Valproic acid. LOD and LOQ values for studied compound were found to be 33.60 and 101.81 µgmL-1, respectively. Mean of recovery values for Valproic acid was 99.40%. The results obtained showed a good agreement with the declared content.

CONCLUSIONS:

No references have been found for optimization study using chromatographic behavior of Valproic acid in pharmaceutical formulation. The difference of this study, combined effect of methanol content and pH of the mobile phase on the retention behavior of Valproic acid was used. The results obtained are of practical importance in the determination of Valproic acid by RPLC, and also are generally useful prediction of effects of pH of mobile phase.

ACKNOWLEDGEMENTS:

This study was supported by a grant of BAP (4934-YL2-17)

P-219: SEPARATION OF ENANTIOMERS OF CHIRAL WEAK ACIDS WITH POLYSACCHARIDE-BASED CHIRAL COLUMNS AND AQUAOUS-ORGANIC MOBILE PHASES IN HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY: TYPICAL REVERSED-PHASE BEHAVIOR

[1] Matarashvili, I., [2] Ghughunishvili, D., [1] Chankvetadze, L., [1] Takaishvili, N., [1] Khatiashvili, T., [2] Tsintsadze, M., [3] Farkas, T., [1] Chankvetadze, B.

[1]Tbilisi State University, Institute of Physical and Analytical Chemistry, School of Exact and Natural Sciences, Tbilisi, Georgia

[2]Georgian Technical University, Faculty of Chemistry, Tbilisi, Georgia

[3]Phenomenex Inc., Torrance, CA, USA

I

NTRODUCTION:

In order to understand the reasons of a dual behavior of polysaccharide-based chiral stationary phases and the role of hydrogen-bonding and of hydrophobic interactions in analyte retention and chiral recognition with these materials, the gradual transition from polar-organic to aqueous-organic mobile phases was investigated with chiral weak acids as test compounds. Special attention was paid to changes in enantiomer elution order.

MATERIALS AND METHODS:

Enantioseparation of chiral weak acids, such as acenocoumarol, benzobamyl, carprofen, 2-(3-chlorophenoxy)-propionic acid, coumachlor, coumatetralyl, difenacoum, fenoprofen, flurbiprofen, halonal, hexobarbital, ibuprofen, indoprofen, ketoprofen, ketorolac, mandelic acid, mandelic acid ethylester, naproxen, Nembutal, 2-phenoxypropionic acid, pyranocoumarin, proglumide, suprofen, sulindac, warfarin, zaltoprofen, was studied by using chiral columns Lux Amylose-1, Lux Amylose-2, Lux Cellulose-1, Lux Cellulose-2, Lux Cellulose-3, Lux Cellulose-4 and chiral column prepared with cellulose tris(3,5-dichlorophenylcarbamate) covalently immobilized on silica in combination with pure polar organic and aqueous-organic mobile phases in high-performance liquid chromatography.

RESULTS:

In the present study additional examples of non-reversed-phase behavior are described in enantioseparations for the first time for weak acidic chiral analytes. In addition, the reversal of enantiomer elution order was observed again for the first time for several analytes based on water-content in the mobile phase.

CONCLUSIONS:

The results represented allow for drawing the following Conclusions:

(1) polysaccharide-based chiral columns when used with aqueous-organic mobile phase may not always behave like typical reversed-phase chromatographic systems; this is especially true at low content of water (<20% v/v) in acetonitrile. (2) When the hydrogen-bonding interactions-based affinity pattern of enantiomers towards a chiral selector is opposite to that based on hydrophobic-type interactions, a reversal of enantiomer elution order may be observed based on the content of water in the mobile phase; this phenomenon seems to be more common in aprotic solvent-water systems than in protic solvent-water systems. Detailed studies on the effect of water addition to organic mobile phase may provide useful information for better understanding of chiral recognition mechanisms with polysaccharide-based chiral selectors.

ACKNOWLEDGEMENTS:

This study was financially supported in part by the Shota Rustaveli National Science Foundation (RNSF) of Georgia, grant No.31/90 for fundamental research.

P-220: ELECTROCHEMICAL DETECTION OF ANTIOXIDANT ACTIVITIES OF 4-INDOLYL-5-OXO-6,6 (OR 7,7)- DIMETHYL-1,4,5,6,7,8-HEXAHYDROQUINOLINE DERIVATIVES

[1] Suslu, I, [2] Simsek, R., [2] Gunduz, MG., [1] Kablan Erdogan, S., [2] Safak, C.

[1]Hacettepe University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

[2]Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

INTRODUCTION:

Antioxidants are the most important species and the play a major role in the protecting biological systems against many diseases. Over the last few years, reasonable supplementations of antioxidants have been widely practiced in different fields of industry and medicine to prevent and delay oxidative stress (1). Antioxidants can inhibit or stop oxidation reactions promoted by free radicals, which are related to DNA degradation, membrane peroxidation and protein denaturation. The reactions promoted by the free radicals lead to the aging process and are also responsible for the occurrence of many diseases such as cancer, diabetes, neurological problems, as well as cardiovascular problems (2). 1,4-Dihydropyridines (1,4-DHPs) are well known as calcium channel modulators. 1,4-DHPs are the most feasible heterocyclic ring with various substitutions at several positions. The present paper is aimed at studying the electrochemical behavior of the 1,4 DHPs by differential pulse voltammetry and hence the assessment of its antioxidant activity from the cathodic reduction peak of oxygen values.

MATERIALS AND METHODS:

All experiments were performed using a Gamry Reference 600 model (Gamry Instruments, PA, USA) potentiostat/galvanostat. A three-electrode system which consisted of disposable pencil graphite electrode (PGE) as working electrode, a Ag/AgCl electrode with saturated 3 M KCl as reference electrode and a platinum wire as counter electrode were used. 0.1 M of tetrabutylammonium iodide salt in 3 mL of dichloromethane solvent was used. The voltammograms were recorded in the conditions of potential range from 0.0 V to -2.0 V vs. Ag/AgCl reference electrode.

RESULTS:

The peak current of oxygen reduction was found to be directly proportional to the 1,4 DHPs concentration in the range of 0.1 - 0.5 mg/mL. The oxygen peak

currents were linearly decreased with increasing concentration of 1,4 DHPs. The coefficient of antioxidant activity (K) of 1,4 DHPs were calculated.

CONCLUSIONS:

Antioxidant properties of the 1,4 DHPs derivative were compared each other.

REFERENCES:

1. Merr PA, Lalitha P, Hemalatha S (2010). Advances in Applied Science Research, 1(3):24-35.
2. Lino FMA et al., (2014). Electrochimica Acta, 128:25-31.

P-221: A NOVEL APPROACH FOR LABEL-FREE GENOSENSING: THE USE OF PENCIL GRAPHITE ELECTRODE MODIFIED WITH GOLD NANOPARTICLES DISPERSED OVER METAL OXIDE FILMS

[1] Aydin, I., [2] Durusoz, H., [1] Ertas, FN, [2] Kara, P.

1. Ege University, Faculty of Science, Department of Chemistry, İzmir, Turkey
2. Ege University, Faculty of Pharmacy, Department of Analytical Chemistry, Izmir, Turkey

INTRODUCTION:

Transition metal oxides have display unique electrocatalytic properties and display strong interactions with noble metal nanoparticles. Pulsed Deposition (PD) provides a high dispersion of the metallic NPs compared to other methods (1). Genosensor technology promises a real time, label free, sensitive and rapid approach for mutation detections as an alternative to conventional methods in microbiological analysis (2).

Genosensors, based on electrochemical transduction of hybridization, have great importance for the detection of pathogen microorganisms, viruses, point mutations in medical applications (3). Such devices couple the high specificity of DNA hybridization reactions with the high sensitivity, low cost and portability of electrochemical transducers (4). Present study describes a novel platform for the genosensing applications depending on AuNP dispersed on transition metal oxides film at a pencil graphite electrode (PGE).

MATERIALS AND METHODS:

The PGE/MeOx/Au electrode was prepared by PD technique where the potential was set at −0.25 V for 5 s and then 1.0 V for 5 s, sequentially for 100 times. Then, the electrode was immersed in Au3+ solution and a similar procedure was applied for 20 cycles. dsDNA was immobilized onto PGE/MeOx/Au surfaces via both adsorption and covalent attachment. The binding of DNA onto PGE/MeOx/Au surfaces were monitored by electrochemical impedance spectrometric (EIS) transduction of the Rct in the presence of 5mM [Fe(CN)6]3-/4-.

RESULTS:

Designed nanogenosensor was performed by evaluating the changes in EIS responses obtained before and after dsDNA immobilized onto, bare, MeOX and MeOx/Au modified surfaces. From the impedance spectra, high charge transfer resistances of PGE/MeOx has shown a sharp decrease after depositing AuNPs onto the surface and this electrode has shown a significant increase after DNA immobilization.

CONCLUSIONS:

This novel electrochemical approach offered a label free, highly sensitive genosensing, with capable of a reliable method for the clinical applications.

REFERENCES:

1. Ozdokur et al., (2016). Sensors and Actuators B, 237:291–297.
2. Garcia et al., (2012). Sensors and Actuators B: Chemical, 161:1030-1037.
3. Kara et al., (2016). J. of Electrochemical Society, 163: 293 -299.
4. Subak H, Ozkan Arıksoysal D (2018). Sensors and Actuators B: Chemical, 263:196 -207.

P-222: ELECTROCHEMICAL INVESTIGATION OF ELETRIPTAN USING GO/PT/IR BASED NANOSENSOR

[1] Kaya, SI., [2] Demirkan, B., [1] Kurbanoglu, S., [2] Kuyuldar, E., [2] Sen, F., [1] Ozkan, SA.

[1]Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

[2]Dumlupinar University, Faculty of Art and Science, Department of Biochemistry, Sen Research Group, Kutahya, Turkey

INTRODUCTION:

Eletriptan (ELE) which is chemically designated as (R)-3-[(1-methyl-2- pyrrolidinyl)methyl]-5-[2-(phenylsulfonyl)ethyl]-1H-indole is a member of drug class named triptans that are used for migraine treatment. ELE is a selective 5-hydroxytryptamine (5-HT1B/1D) receptor agonist and highly effective for relieving or reducing severeness of migraine headaches. Graphene which is an allotrope form of carbon has hexagonal configuration of sp2 hybridized carbon atoms. Due to its great ability to promote electron transfer, great catalytic behavior toward small compounds and high surface area; graphene is widely used in electrochemical sensing. Graphene oxide (GO) has a similar structure to graphene but the layers of GO have oxygen-containing groups. Metal nanoparticles, such as gold, platinum, palladium, are materials which have sizes ranging from 1 to 50 nm. Due to their unique physical, chemical and electronic properties; metal nanoparticles modified electrodes show faster redox activity towards compounds compared to bare electrodes. The aim of the present

work is to investigate the voltammetric behavior and determination of ELE in pharmaceuticals using platinum and iridium nanoparticles and graphene oxide modified GCE (GO/Pt/Ir/GCE) nanosensor.

MATERIALS AND METHODS:

The 1×10−3 M stock solution of ELE was prepared in methanol. The working solutions of ELE were prepared daily by accurate dilution with pH desired buffer solution containing 20% methanol. In this study; pH 0.3,0.5 M and pH 0.5, 0.1 M H2SO4 solutions, pH 1.5, pH 2.5, pH 3, pH 6.02, pH 6.5, pH 7.0 and pH 8.0 phosphate buffer (PB) solutions, pH 3.7, pH 4.7 and pH 5.7 acetate buffer solutions were used as supporting electrolyte for the effect of pH studies. The GO/Ir/Pt suspension was prepared by dispersing 1 mg of GO/Ir/Pt in 1 mL distilled water and the suspension ultrasonicated for 2hours using ultrasonic bath. Before the modification, the surface of bare GCE was polished with alumina slurry on a polishing cloth then washed with distilled water and dried. Different volumes of GO/Ir/Pt suspension was dropped to electrode surface and dried in a vacuum oven.

RESULTS:

The pH of the supporting electrolyte has a significant influence on the oxidation peak potentials and peak currents of ELE. The influence of the pH was studied using H2SO4 solutions, acetate and phosphate buffers in the pH range between 0.3 and 8.0 by DPV and OSWV. With increasing pH; the Ep shifted to less positive values. Ep showed linear response versus pH. The equations above and the Ep versus pH plot indicate that the Ep is pH dependent. Moreover, since the slope values are close to theoretical value of -59 mV equal amounts of electrons and protons may involve in the rate-determining steps. LOD value confirmed the sensitivity of the proposed method which was found as 4.46 × 10-7 M.

CONCLUSIONS:

In this study, the voltammetric behavior and determination of ELE in pharmaceutical dosage forms were investigated using GO/Pt/Ir/GCE nanosensor by DPV. The effect of various parameters such as pH, scan rate and nanomaterial amount were also studied. The electrochemical process was found irreversible, pH dependent and controlled by the adsorption of ELE onto the electrode. The results showed that the GO/Pt/Ir/GCE nanosensor significantly enhanced the oxidation peak current of ELE and also revealed a shift of peak potential of ELE to less positive values due to electrocatalytic effect compared to bare electrode using DPV.

REFERENCES:

1. Katzung BG, Trevor AJ (2015). Basic & Clinical Pharmacology, 13th ed.
2. Wang J (2005). Analyst. 130:421–426.

P-223: DEVELOPMENT AND VALIDATION OF GREEN CAPILLARY ELECTROPHORETIC METHOD FOR DETERMINATION OF GLIBENCLAMIDE IN PHARMACEUTICAL DOSAGE FORMS

[1] Sanli, S., [2] Sardogan, S., [3] Palabiyik, IM, [2] Sanli, N.

[1]Usak University, Faculty of Science and Arts, Department of Chemistry, Usak, Turkey

[2]Usak University, Faculty of Engineering, Department of Food Engineering, Usak, Turkey

[3]Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

To resolve environmental pollution problem, scientific studies have recently focused upon the development of environmentally friendly or green processes, methods and techniques. These methods, applications and techniques are known as green chemistry (1). Glibenclamide is the most extensively used sulphonylurea in many parts of the world for the management of non-insulin-dependent diabetes mellitus (NIDDM) (2).

MATERIALS AND METHODS:

All studies were performed on a Agillent Capillary Electrophoresis System with a diode array detector. A 55 cm × 50 μm i.d. fused silica capillary (Polymicro Technologies, Tucson, AZ) with an effective length of 45 cm was used. Buffer, containing 20 mM Na2B4O7, was adjusted to pH 6.0 with 0.5 M H3BO3. The Applied voltage was 30 kV, pressure injection was at 10 psi for 5 s, and the detection was performed at 230 nm.

RESULTS:

Under these conditions, retention times of glibenclamide is 2.5 minute. Linearity range is between 1 – 12 ppm. LOD and LOQ values were calculated as 0.054 and 0.164 ppm. Relative Standard deviations (%) and recovery (%) values were calculated for 4 and 8 mg/L glibenclamide in intra day as 0.123 % and 99.99 % and 0.674 % and 99.99 %. This developed method was applied to analysis of glibenclamide in a pharmaceutical dosage form

CONCLUSIONS:

A simple, rapid, precise and environmentally friendly capillary electrophoresis method for the determination of glibenclamide in pharmaceutical dosage form.

ACKNOWLEDGEMENTS:

This study was supported by a project of BAP of Uşak University (2014MF008)

REFERENCES:

1. Koel M, Kaljurand M (2006). Pure Appl Chem., 78:1993–2002.
2. Nanovskaya T, Nekhayeva Hankins G, Ahmed M, (2006). BioChem Pharmacol.,72: 632-639.

P-224: GOLD NANOPARTICLES MODIFIED SCREEN PRINTED ELECTRODE FOR SENSITIVE DETECTION/ENHANCED SENSING OF ANTICANCER DRUG IRINOTECAN-DNA INTERACTION

[1,2] Shahzad, S., [2] Kurbanoglu, S., [2,3] Karadurmus, L., [1] Shah, A., [2] Ozkan, SA.

[1]Quaid-i-Azam University, Department of Chemistry, Islamabad, Pakistan

[2]Ankara University, Department of Analytical Chemistry, Ankara, Turkey

[3]Adiyaman University, Department of Analytical Chemistry, Adiyaman

INTRODUCTION:

The clinical pharmacokinetic profile of irinotecan has always attracted researchers to explore the use of this anticancer drug. In high dosage this drug causes problems like severe diarrhea, abdominal cramping and nausea. It is important to develop a sensitive sensor which can detect minute amounts of Irinotecan. Electrochemical biosensors have received great attention due to their easy fabrication, reduced the attempts to manipulate the surface of sensor chips utilizing nanomaterials to enhance the sensing signals especially metallic nanoparticles. In this work gold nanoparticles (AuNPs) were used to develop a sensitive nanobiosensor to detect DNA –Irinotecan interaction.

MATERIALS AND METHODS:

AuNPs were used to modify electrode by using two strategies. A mixture of DNA and gold nanoparticles was deposited on electrode and its response was measured in acetate buffer of pH 4.65. In other case layer of gold nanoparticles was deposited and dried at room temperature followed by DNA layer deposition. Different concentrations of AuNPs were dropped on the surface of SPE and air dried to know the optimized concentration. The optimized amount obtained was 10 µL of AuNPs with 5 µL drop on surface of electrode left to air dry followed by another 5 µL drop of AuNPs. After 15 µL of dsDNA were dropped on the surface and the response was measured via differential pulse voltammetry

RESULTS:

The developed modified nanobiosensor was interacted with Irinotecan and a remarkable decrease in the guanine signal of DNA was observed as compared to unmodified sensor. The low intensity peak signal was attributed to DNA condensation caused by irinotecan. This result was further validated by poly guanine and spectrophotometric studies.

CONCLUSIONS:

A disposable screen printed modified nanobiosensor was developed to sense the electrochemical response of irinotecan-DNA interaction.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK – 2216 programme.

P-225: ELECTROCHEMICAL NANOSENSOR FOR THE ELECTROCHEMICAL INTERACTION OF IDARUBICIN WİTH DNA

[1,2] Karadurmus, L., [1] Kurbanoglu, S., [3] Shah, A., [1] Ozkan, SA.

[1]Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

[2]Adiyaman University, Faculty of Pharmacy, Department of Analytical Chemistry, Adiyaman, Turkey

[3]Quaid-i-Azam University, Chemistry Department, Islamabad, Pakistan

INTRODUCTION:

Idarubicin (IDA) is an antineoplastic in the anthracycline class. IDA is a DNA-intercalating analog of daunorubicin which has an inhibitory effect on nucleic acid synthesis and interacts with the enzyme topoisomerase II. IDA intercalates into DNA and interferes with the activity of topoisomerase II, thereby inhibiting DNA replication, RNA transcription and protein synthesis. Due to its high lipophilicity, IDA penetrates cell membranes more efficiently than other anthracycline antibiotic compounds. Drug–DNA interaction studies can give us brief information about the mechanism of the drug in the human body.

MATERIALS AND METHODS:

Electroanalytical methods are widely used in drug analysis, due to high sensitivity and selectivity, their low cost, reagents consumption and relatively short analysis time. Subsequently the use of chemically modified electrodes as electrochemical sensors have been highly recommended, as they since the modification enhances electron transfer rate and the sensitivity of working electrode by decreasing the redox potential of analyte (1). Nowadays, nanomaterials are generally used in designing nanobiosensors due to their high surface area, good mechanical properties,

inertness etc. Especially, silver nanoparticles (AgNPs) and platinum nanoparticles (PtNPS) are reason of choice depending on their biocompatibilities.

RESULTS:

In this study, an electrochemical DNA-based biosensor was developed for the detection of DNA–IDA interaction through the electroactive properties of guanine and adenine nucleotides. Interaction time, nanoparticle amount (AgNPs, PtNPs), modification strategy and concentration of drug in response to guanine were optimized

CONCLUSIONS:

Layer-by-layer modification of the screen-printed electrode-based DNA biosensor gave the highest guanine response and resulted in a well-followed decrease in guanine signal after interaction with 0.5 ppm IDA. With 5 min interaction time, the SPE/PtNPs/AgNPs/AgNPs DNA biosensor gave a linear response between 0.05 and 1.0 ppm IDA.

REFERENCES:

1. Ozkan SA. Electroanalytical Methods in Pharmaceutical Analysis and Their Validation. HNB Publishing, New York, 2

P-226: EVALUATION OF CHIRAL STATIONARY PHASES PREPARED BY COVALENT IMMOBILIZATION OF CELLULOSE 3,5-DICHLOROPHENYLCARBAMATE ON CORE-SHELL SILICA

[1] Bezhitashvili, L., [1] Bardavelidze, A., [1] Kakava, R., [2] Gumustas, M., [3] Ozkan, SA., [1] Chankvetadze, B.

[1]Tbilisi State University, Faculty of Exact and Natural Sciences, Department of Chemistry, Tbilisi, Georgia

[2]Ankara University, Institute of Forensic Sciences, Department of ForensicToxicology, Ankara, Turkey

[3] Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

The chromatographic separation of enantiomers is one of the most difficult challanges in analitical chemistry. The advantages of superficially porous silica (SPS) over fully porous silica (FPS) chiral separations are documented (1). Shorter diffusion path-length and consequently higher column efficiency belong to the major advantages of these materials as well as to a lesser extent more uniform particle-size distribution of core–shell particles compared to their totally porous analogues.The aim of present work is to evaluate chiral columns prepared by covalent immobilization of cellulose 3,5-dichlorophenylcarbamate on core-shell silica for separation of enantiomers in high-performance liquid chromatography (HPLC).

MATERIALS AND METHODS:

In the frame of this study, enantioseparation of seven chiral sulfoxides including 2-(benzylsulfinyl)-benzamide, 2-(benzylsulfinyl)-N-methyl benzamide, 2-(benzylsulfinyl)-N,N-dimethyl benzamide, 2-(3-bromo-benzylsulfinyl)-benzamide, 2-(2-methyl -benzylsulfinyl) benzamide, 2-(3-methyl-benzylsulfinyl) benzamide and 2-(4-methyl-benzylsulfinyl) benzamide were performed with varying flow rates of mobile phase from 0.1 to 5.0 mL/min. Polar organic solvents like methanol and acetonitrile were used as mobile phases. The effect of the detection frequencies of 5 and 160 Hz were also compared.

RESULTS:

High separation potential of SPS-based CSPs and high column efficiency was demonstrated, both at the optimal flow rate of the mobile phase as-well-as at the highest possible flow-rate of the mobile phase provided by the instrumentation used in this study. The difference in plate counts estimated at optimal and at instrument imposed maximal flow rates was small.

CONCLUSIONS:

The results of this study indicate that a combination of polysaccharide based chiral selectors with superficially porous silica is a very useful approach for the preparation of chiral stationary phases for fast and highly efficient separations of enantiomers in HPLC. Even working with higher flow rates (5.0 mL/min), highly efficient separation of enantiomers can be achieved with the analysis time in the range between 15-30 seconds.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Mevlana exchange program with the project number MEV-2017-52

REFERENCES:

1. Bezhitashvili L et al., (2017). J. Chrom. A., 1482:32–38.

P-227: SEPARATION OF ENANTIOMERS OF NOVEL CHIRAL PYRAZOLINE DERIVATIVES IN HPLC WITH POLYSACCHARIDE BASED CHIRAL COLUMNS BY USING POLAR ORGANIC MOBILE PHASES

[1,2] Gumustas, M., [3] Bezhitashvili, L., [4] Gokhan Kelekci, N., [2] Ozkan SA., [3] Chankvetadze, B.

[1]Ankara University, Institute of Forensic Sciences, Department of Forensic Toxicology, Ankara

[2]Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara

[3]Tbilisi State University, School of the Exact and Natural Sciences, Institute of Physical and Analytical Chemistry, Tbilisi

4Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara

INTRODUCTION:

Separation of enantiomers is a hot topic for academic research, as well as in modern pharmaceutical industry. The reason for this is that more than 50 % of the small molecule drugs currently in use are chiral compounds and significant part of them are racemates consisting of an equimolar mixture of two enantiomers. Chiral pyrazoline derivatives are in general well-known five-membered nitrogen-containing heterocyclic compounds. In this study, relationships between structure of chiral analytes on one hand, and the nature of chiral selector and mobile phase on the other hand were investigated.

MATERIALS AND METHODS:

Recently synthesized 41 pyrazoline derivatives (1) were used in this study. HPLC grade acetonitrile and methanol were acquired from Sigma Aldrich. Commercially available chiral columns of Lux series from Phenomenex Inc. (Torrance, CA, USA) namely Lux Cellulose 2 and Lux Cellulose 3 with the dimensions 4.6x250 mm and 3 µm and Lux Cellulose 4 with the dimension 4.6x250 mm and 5 µm were used. The Agilent Technologies HP 1200 series (Santa-Clara, CA, USA) LC system was equipped with a degasser, quaternary pump, auto sampler and diode array detector was used in the present study. HPLC separations were performed at room temperature with 1 mL/min mobile phase flow rate.

RESULTS:

In order to achieve this goal, the enantiomers of 41 chiral pyrazoline derivates were separated by using polysaccharide based chiral columns and polar organic mobile phases in HPLC.

CONCLUSIONS:

As this study illustrates, the affinity of enantiomers of chiral pyrazoline derivatives towards polysaccharide-based chiral stationary phase is dependent on the nature of the polar organic mobile phase (2). Further studies in this direction may provide useful information for understanding the chiral recognition mechanisms with polysaccharide-based chiral stationary phases.

ACKNOWLEGEMENT:

This study was partially supported by Mevlana International Exchange Program with the project number MEV-2017-52.

REFERENCES:

1. Gökhan Kelekci N et al., (2007). Bioorganic and Medicinal Chemistry, 15:5775-5786.
2. Chankvetadze B. (2012). J. Chromatogr. A, 1269:26.

P-228: REDUCTION MECHANISM AND ELECTROCHEMICAL DETERMINATION OF OF RISPERIDONE

[1] Baymak, MS., [2] Celik, H.

[1]Marmara University, Faculty of Science and Art, Department of Chemistry, Istanbul, Turkey

[2]Yeditepe University, Faculty of Pharmacy, Department of Analytical Chemistry, Istanbul, Turkey

INTRODUCTION:

Schizophrenia is one of the most frequently seen physiologic diseases in many countries and affects 1.1% of the world's population. It comes with many negative symptoms such as thinking disorder. Drugs in the market today are not effectively sufficient to cure the disease, they only regulate the symptoms. Risperidone, with active ingredient4-[2-[4-(6-fluorobenzo[d]isoxazol-3-yl)-1-piperidyl]ethyl]-3-methyl-2,6-diazabicyclo[4.4.0]deca-1,3-dien-5-one , is one of these drugs and can be prescribed to youths in the age of 13-18 which makes up for the its most remarkable feature. The analytical determination of the drug have been studied mostly with chromatographic methods including HPLC (1,2), liquid chromatography in combination with UV detection (3), capillary zone electrophoresis and first order derivative spectrophotometry (4). On the other hand, application of electrochemical methods in pharmaceutical formulations was achieved in two studies using differential pulse polarography (5) and square-wave cathodic adsorptive stripping voltammetry (6). Even though an attempt to identify the electroactive grouping on the molecule was made by cyclic voltammetry (7), a mechanism for the reduction of the compound was not proposed.

MATERIALS AND METHODS:

In this study, the solution chemistry of Risperidone has been investigated by the aid of polarography. The electrochemical behavior of Risperidone is compared with that of OH-Risperidone. Simple buffer systems were used with pH values between 1 and 12 and the chemicals used to prepare these buffer solutions were of analytical grade.

RESULTS:

The purpose was to elucidate the electron transfer mechanism of Risperidone in different pH ranges and propose a mechanism for its reduction. DC Polarography is used for this purpose since it is one of the most informative methods for such investigations. DP Polarography was used for determination purposes. This method is easy to apply for such formulations and requires no pre-treatment of the metabolites. The calculated validation parameters are as follows: LOD: 1.9x10-7; LOQ: 6.5x10-7; Slope of the calibration curve: 46504.

Conclusion: The electron transfer mechanism of Risperidone has been elucidated at different a pH ranges. Another contribution of this study lays in a proposed electrochemical method for its determination by using DP Polarography.

REFERENCES:

1. Olesen OV, Linnet K(1997). J.Chromatogr.,B:Biomed.Sci.Appl., 698: 209-216.
2. Price MC, Hoffman DW (1997). Therap.Drug Monit., 19:333-337.
3. Avenoso A, Faccida G, Salemi M, Spina E (2000). J.Chromatogr.,B:Biomed.Sci.Appl., 746:173-181.
4. Lui X, Fu C, Li L, Wang X (2001). Zhongguo Yiyao Gongye Zazhi, 32:174-178.
5. Jeyaseelan C, Jugade R, Joshi AP (2006). Croatica Chemica Acta, 79(4):541-544.
6. Tasdemir IH, Cakirer O, Erk N, Kilic E (2011). Collect.Czech.Chem.Commun., 76(3):159-176.
7. Cakirer O, Tasdemir IH (2010). Asian J.Chem. 22(8):6353-6365.

P-229: PREPARATION OF A NEW BIOSENSOR BASED ON GRAPHENE FOR GLUCOSE DETERMINATION

[1] Oncul, MA., [2] Cete, S., [2] Yasar, A.,

[1]. Gazi University, Institute of Sciences, Department of Chemistry, 06500 Ankara, Turkey

[2]. Gazi University, Faculty of Sciences, Department of Chemistry, 06500 Ankara, Turkey

INTRODUCTION:

Glucose is one of the main molecules that act as an energy source for the human body. In addition, living cells use glucose as a metabolic intermediate in the synthesis of more complex molecules such as fats (1). The significance of glucose in human metabolism is well known, as is the fact that the defects in glucose level lead to complications of diabetes (2).

MATERIALS AND METHODS:

The glassy carbon electrode surface was covered with a platinium nanoparticle graphene solution by dropping. The glucose oxidase enzyme was immobilized by cross-linking on the electrode modified by graphene / platinium nanoparticles / nafion solution. Optimum conditions of GR / PtNps / Nf film and biosensor were determined. The linear working range of biosensor for glucose was determined. The effects of pH and temperature on the response of the glucose biosensor were investigated. Reusability and storage stability were determined of the biosensor.

RESULTS:

Linear working range of prepared biosensor was determined 5 μM to 50 μM. The activitiy of biosensor was maintained 94.5% at the end of 20 measurements. The values of Km and Vmax for the GR / PtNps / Nf-GOD enzyme electrode system were found to be 0,94 mM and 0,775 μA / min, respectively. The optimum pH and temperature values for glucose biosensor were found 8.0 and 50 °C.

CONCLUSIONS:

Electrochemical studies show GR / PtNps / Nf film can provide a biocompatible and electrochemical microenvironment for immobilization of enzyme, making this material a good candidate for the fabrication of highly sensitive and selective glucose biosensors.

REFERENCES:

Fang B, Zhan C, Wang G, Wang M, Ji Y (2011). Sensors and Actuators B: Chemical 155:304-310.

Shankaran DR, Uehara N, Kato T (2008). Biosensors and Bioelectronics 18:721–728.

P-230: EFFECT OF PARTICLE SIZE AND PARTICLE SIZE DISTRIBUTION ON MONTELUKAST SODIUM DISSOLUTION

Dalkiran, M., Akkoyun Muhiddin, O., Seyidoglu Koksal, A., Usluer, O., Acar Karakoy, B., Onuk Goren, F.

Pharmactive Ilaç San. ve Ticaret A.S. Tekirdag, Turkey

INTRODUCTION:

The aim of the study is to examine the effect of particle size and particle size distribution on Montelukast Sodium dissolution. Montelukast Sodium is a leukotriene receptor antagonist,is used commercially as a maintenance treatment for asthma and to relieve allergic symptoms (1). According to physicochemical characterization Montelukast Sodium is defined as a Class II molecule in BSC (biopharmaceutical classification).It has low solubility and high permeability.Increasing the effectiveness of the Montelukast sodium depends on the rate of dissolution of the molecule since it is a Class II molecule. Most important parameters affecting the solubility are the particle size and particle size distribution of the active substance.

MATERIALS AND METHODS:

In this study the effect of different particle size distributions on solubility has been investigated. Active substance particle size distribution results obtained by using a Malven Masterizer 3000 laser light scattering method and supplied from the same supplier are presented in Table 1 below.

Table 1: Montelukast Sodium Particle Size Distribution

Montelukast Sodium Particle Size Distribution (µm)			
	D10	D 50	D90
11001-161001	4.42 µm	18.9 µm	77.9 µm
11001-170602 (micronized)	1.8 µm	9.2 µm	35.5 µm

Solubility studies of tablets manufactured with the API lot number 11001-161001 and 11001-170602 (micronized) were performed by using a validated dissolution method;which is 900 mL of 0.5% SDS at a rotation speed of 50 rpm(USP Pallet).

RESULTS:

A profile dissolution study was performed at 10th minute,15th minute,20th minute,30th minute,45th minute and 60th minute.Dissolution and RSD values have been calculated as 78% and 7.4% respectively for the product manufactured with the API lot numbered 11001-161001,at 15th minute. When the product is manufactured with the 11001-170602 lot numbered micronized API dissolution and RSD results have been calculated as 94% and 4.3% at 15th minute. When compared with the reference product which have 94% dissolution and 2% RSD value it can be concluded that test product manufactured with micronized API is similar to reference product. It has been proved with this study that the efficiency of the dissolution rate profile has increased as the particle size reduced and the product becomes similar to the reference product.

CONCLUSIONS:

Micronized active substance is preferred for use in product formulations.

REFERENCE:

1. Shin IS et al., (2013). International Immunopharmacology, 17:867–873.

P-231: INVESTIGATION OF THE EFFECT OF COMMERCIAL HERBAL MIXTURE ON HEPG2 LIVER CANCER CELL LINE BY PROTEOMIC APPROACH

[1,2] Nenni, M., [3] Oncul, S., [3] Ercan, A., [1] Suslu, I., [1] Celebier, M., [4] Haznedaroglu, IC.

[1]Cukurova University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

[2]Hacettepe University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

[3]Hacettepe University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey

4Hacettepe University, Faculty of Medicine, Department of Hematology, Ankara, Turkey

INTRODUCTION:

Recent reports indicate that liver cancer is one of the most prevalent malignancies in both men and women worldwide (1). The anticancer effect of the components of commercial herbal mixture (CHM) on various cancer types is well known and previously been investigated by proteomic studies. Two-dimensional (2-D) gel electrophoresis is the first step in the classical proteomic strategy to resolve the complex nature of cellular content. The procedure combines two types of gel electrophoresis: pI based protein separation by isoelectric focusing (IEF), and molecular weight separation by SDS-PAGE (2, 3).

MATERIALS AND METHODS:

In this study, HepG2 liver cancer cell line was chosen for proteomic analysis. Cells treated with CHM (Group T) were compared to the control (Group C). Cytosolic fractions of proteins in group T and C were separated by 2-D gel electrophoresis. SYPRO Ruby was used for gel staining. The 2-D gels were scanned and the relative gel images were analyzed using PDQuest software. After image filtration for background removal, spots were automatically detected and manually edited. PDQuest was used for the statistical analysis and selection of the up or downregulated proteins in both groups.

RESULTS:

The PDQuest detected an average of 298 spots for two groups. Then, PDQuest software defined ‘t-test’ and ‘Quant’ group, where t-test was the proteins statistically identical in the same group regarding their spot intensities and the Quant group comprised of proteins having 2-fold change amongst the groups T and C. The intersection of these groups was detected to be 88 spots.

CONCLUSIONS:

According to proteomic studies, CHM changes the level of certain proteins in HepG2 cells. To determine whether overexpressed and under expressed proteins are associated with anticancer activity, spot should

further be analyzed by MALDI-TOF MS and identified by peptide mass fingerprint.

REFERENCES:

1. Bosch FX et al., (2004). Gastroenterology, 127(5): S5-S16.
2. Liu H et al., (2013). Journal of Proteome Research, 12(3): 1300-1315.
3. Rabilloud T et al., (2007). Plant Proteomics: Methods and Protocols, 111-119.

P-232: IDENTIFICATION OF ORGANOCHLORINE PESTICIDES (OCPS), IN SPIKED COMMERCIAL COW MILK SAMPLES BY GC-MS

[1,2] Nenni, M., [1] Zeki, OC., [1] Suslu, I., [1] Celebier, M., [1] Altinoz, S.

[1]Hacettepe University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

[2]Cukurova University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Milk-producing animals (cows) accumulate residues of these insecticides through contaminated feed, grass and inhaled air. Due to their lipophilic properties, OCPs are primarily stored in fat-rich tissues and subsequently translocated and excreted through milk fat (1). The evidence of organochlorine hormone-disruption activity has been reported. This fact has caused concern since milk and dairy products play a central role in human nutrition (2). The aim of this study is to develop an analysis technique for identification of 6 different OCPs (1 ppm β-HCH, δ-HCH, 4,4'DDT, 4,4'DDD, 2,4'DDD and 4,4'DDE) in spiked commercial cow milk samples by GC-MS.

MATERIALS AND METHODS:

Commercial cow milk samples were extracted by using liquid–liquid extraction. After extraction, supernatant was dried with vacuum centrifuged and dissolved by adding hexane (The process was done to increase the OCPs concentration in the sample). Then they were injected into the GC-MS system where an Agilent J&W DB-624UI (e.g., plot columns) was used. The injector temperature was 250°C, the purge flow was 5 mL.min-1, and the column temperature was held at 60°C for 1 min, then the increased to 325°C and held there for 10 min. The interface and the ion source temperatures were 230 and 290°C, respectively. Ions were generated by a 70-eV electron beam. A more detailed overview presenting separate data for OCPs given Table1.

Table1. Identification parameters by GC-MS

OCPs	Migration Time	Fragment Ions(m/z)
β-HCH	17.965	109, 181, 183
δ-HCH	17.025	109, 181, 183
4,4'DDT	24.736	235, 237, 165
4,4'DDD	22.946	235, 237, 165
2,4'DDD	24.031	235, 237, 165
4,4'DDE	22.244	246, 248, 316

RESULTS:

In this procedure, which combines liquid-liquid extraction technique with GC-MS, a qualitative assay of 6 different OCPs was made from commercial cow milk.

CONCLUSIONS:

It is important to know what the exposure agent is so that the correct treatment can be applied to the exposure to the pesticides. For this purpose, qualitative analysis of spiked milk samples of OCPs was performed by using a GC library, suggesting a procedure that combines liquid-liquid extraction technique with GC-MS.

REFERENCES:

1. Bentabol A et al., (1995). Pestic Science, 44:177-182.
2. Colbom T (1993). Environ Health Perspect, 101:378-384.

P-233: A COMPARISON BETWEEN EXPERIMENTAL AND THEORETICAL SPECTROSCOPIC DATA OF GATIFLOXACIN

Mimouni, FZ., Belboukhari, N., Sekkoum, K.

Tahri Mohamed University, Bioactive Molecules & Chiral Separation Laboratory, Bechar, Algeria

INTRODUCTION:

Fluoroquinolones constitute an essential class of antibacterials, and widely used in clinical applications. This study describes the spectroscopic and theoretical investigation of Gatifloxacin. The experiment results were performed with IR spectroscopy, UV- visible spectroscopy and NMR spectroscopy.

MATERIALS AND METHODS:

Theoretical calculations were performed with Gaussian 16 and GaussView 6 software Packages. The geometry optimization of structure, and vibrational frequencies of Gatifloxacin (GATI) have been calculated by density functional theory DFT-B3LYP methods with the 6-31++G(d,p) basis set. The Mulliken atomic charges of our molecule were also performed using the DFT method.

RESULTS AND CONCLUSION:

The presented spectroscopic investigations on GATI shows the good agreement between observed spectra and theoretical predictions of the drug. In IR spectra, the difference in intensities is seen may be due the intramolecular H-bonding in experimental study. In the experimental and theoretical studies of UV absorption energy of GATI are almost similar. For the 1H NMR observed and theoretical predicted spectra are shows the same results.

ACKNOWLEDGEMENTS:

Authors gratefully acknowledge the management Tahri Mohamed University, Bechar, Algeria, for encouraging and providing necessary facilities for carrying out this work.

REFERENCES:

1. Riahi S et al. (2009). Materials Science and Engineering: C, 29(6):1808-1813.
2. Kłosińska Szmurło E et al. (2014). Journal of Biological Physics, 40(4):335–345.
3. Shamoon AS et al. (2012). Spectroscopy: An International Journal, 27 (23):185–206.
4. Frisch MJ et al. (2016). Gaussian 16W, Version 1.1, Gaussian, Pittsburgh, Pa, USA.
5. Sanası PD et al. (2013). Scientia Pharmaceutica, 81(1): 651–662.

P-235: DETERMINATION OF RIVAROXABAN IN TABLETS USING ULTRA HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

[1,2] Kozanli, M., [1,2] Can, NO.

[1]Anadolu University, Faculty of Pharmacy, Department of Analytical Chemistry, Eskisehir, Turkey

[2]Anadolu University, Faculty of Pharmacy, Doping and Narcotic Compounds Analysis Laboratory, Eskisehir, Turkey

INTRODUCTION:

Rivaroxaban (RIV) is an oral oxazolidinone-based anticoagulant and a potent and selective direct inhibitor of factor Xa; mainly, RIV is in use for the prevention of venous thromboembolism in adult patients (1). The aim of this study was to develop a new liquid chromatography method for determination of RIV in tablets.

MATERIALS AND METHODS:

Analysis were performed using a Nexera-i series of ultra high performance liquid chromatography (UHPLC) system from Shimadzu (Japan). Escitalopram (ESC) was used as an internal standard (IS). The separation was performed by a C18 bonded fused-core silica column (Phenomenex Kinetex® 2,6 µm, 150x4.6 mm). The mobile phase was consisted of water, acetonitrile and methanol (55:20:25, v/v/v), which was pumped at 0.5 mL/min flow-rate. The analytes were injected as 10 µL aliquots and detected using a photodiode array detector set at 249 nm. The method was validated according to ICH Q2(R)1 regulations (2), and system suitability parameters were checked according to USP.

RESULTS:

Conventional chromatographic parameters were investigated for optimization of method such as organic solvent ratio, flow rate, injection volume etc. Retention times of RIV and ESC were observed as 3.90 and 6.40 min respectively; total runtime was 8 min. Analysis of RIV was achieved with very high efficiency; the number of theoretical plates were about 19600 and 12200 for RIV and ESC, respectively. Isocratic elution of RIV was successful with observing good system suitability values. Capacity factor was about 2.2 for RIV and 4.2 for ESC; on the other hand tailing factor of RIV peak was 1.2, while it was 1.9 for ESC. Besides, effects of mobile phase composition and detection wavelength on the retention time and signal intensity was evaluated.

CONCLUSIONS:

A simple, rapid, accurate and precise UHPLC method has been developed and validated for the routine quantitative analysis of RIV in tablets.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Anadolu University Scientific Research Projects Commission (Project No: 1703S083).

REFERENCES:

1. Duggan, ST (2012). Rivaroxaban; American Journal of Cardiovascular Drugs, 12(1): 57–72.
2. ICH Harmonised Tripartite Guideline(2005). Validation of Analytical Procedure Text and Methodology Q2 (R1)

P-236: THE EFFECT OF POLYCATIONIC AMPHIPHILIC CYCLODEXTRIN NANOPARTICLES ON MDA-MB CANCER CELLS: A METABOLOMIC APPROACH TO UNDERSTAND THE MECHANISM

[1] Celebier, M., [1] Kaplan, O., [1] Varol, I., [2] Varan, G. [3] Oncul, S., [1] Kocak, E., [3] Ercan, A., [2] Bilensoy, E.,

[1]Hacettepe University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

[2]Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

[3]Hacettepe University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey

INTRODUCTION:

Metabolomics is the scientific study of chemical processes involving metabolites. Specifically, metabolomics is the "systematic study of the unique chemical fingerprints that specific cellular processes leave behind", the study of their small-molecule metabolite profiles (1). In this study, a metabolomic approach was performed to understand the effect of amphiphilic cyclodextrin nanoparticles on MDA-MB cancer cells.

MATERIALS AND METHODS:

Control group (Group C) of MDA-MB cells were compared with the one treated with the amphiphilic cyclodextrin nanoparticles (Group T). Metabolomic studies were carried on Q-TOF LC/MS. Metabolites in cytosolic fractions were purified by ultrafiltration method and separated by Zorbax HILIC Plus chromatography column. XCMS on-line (2) was used to find the metabolites affected by cyclodextrin nanoparticle treatment.

RESULTS:

Mainly 2758 and 208 peaks were found by using XCMS centwave and matchedFilter algorithims, respectively. However, 15 peaks having fold change more than 2 and statistically significant ($p<0.05$) were the intersection of these algorithms. These peaks were matched with metabolites by using Human Metabolome Database (HMDB) and it was found the some of the affected metabolites were involved in cancer metabolism.

CONCLUSIONS:

According to the results, it could be concluded that metabolomics is one of the key strategy to understand the effect of small molecules on cancer cells. Various algorithms to identify the metabolite peaks in chromatograms provide identical results after statistical analysis.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-115S456)

REFERENCES:

1. Baker M (2011). Nature Methods, 8:117-121
2. Tautenhahn R, Patti GJ, Rinehart D, Siuzdak G (2012). Analytical chemistry, 84:5035-5039.

P-237: ENANTIOSEPARATION OF 4 IMINOFLAVAN DERIVATIVES ON POLYSACCHARIDE BASED CHIRAL STATIONARY PHASES BY HPLC

[1] Rahou, I., [1] Belboukhari, N., [1] Sekkoum, K., [1] Bounoua, N.,[2] Cheriti, A., [3] Aboul Enein, HY.

[1]University of Tahri, Faculty of Science and Technology, Mohamed Bioactive Molecules and Chiral Separation laboratory, Bechar, Algeria

[2]University of Tahri Mohamed, Faculty of Science and Technology Phytochemistry and Organic Synthesis Laboratory, Bechar, Algeria

[3]Pharmaceutical and Drug Industries Research Division, National Research Center, Pharmaceutical and Medicinal Chemistry Department, Dokki, Egypt

INTRODUCTION:

The reactivity of the flavonoids' C4 carbonyl led to synthesis of new chiral products of iminoflavan derivatives, and our work is concentrated on the chiral separation of these molecules by liquid chromatography on six polysaccharide-based CSPs under polar and normal organic phase modes (1-3).

MATERIALS AND METHODS:

4-iminoflavans was successfully accomplished in the normal phase mode using six polysaccharide-based chiral stationary phases namely, Chiralcel®OD-H, Chiralcel®OD, Chiralcel®OJ, Chiralpak®AD, Chiralpak®IA and Chiralpak®IB under normal and polar organic phase modes.

RESULTS:

The resolution depended on nature and concentration of alcoholic modifer. The results demonstrate clearly that the chromatographic system based on the coated and immobilized type Chiralpak®IB and Chiralcel®OD-H CSPs provide a powerful analytical tool for enantiomeric separation of all the 4-iminoflavans used in this study.

CONCLUSIONS:

A chiral HPLC method for the separation of eight racemic aryl iminoflavanone derivatives was developed. The separation was successfully performed on the six polysacharride-based chiral stationary phases under normal and polar organic phase modes.

REFERENCES:

1. Belboukhari N (2012). J Chromat Separation Techniq., 3:67–68.
2. Lahmer N et al., (2011). Phytochem Biosub J., 5:13–18.
3. Ye YK, lynam KG, Stringham RW (2006). Chirality, 18:1–9.

P-238: A NOVEL LC-MS/MS METHOD FOR DETERMINATION OF TASIMELTEON

[1,2] Can, NO., [1,2] Ozcan, S., [2,3] Levent, S., [1,2] Kozanli, M. [2,3] Ozkay, Y., [3] Kaplancikli, ZA.

[1]Anadolu University, Department of Analytical Chemistry, Faculty of Pharmacy, Eskisehir, Turkey

[2]Anadolu University, Faculty of Pharmacy, Doping and Narcotic Compounds Analysis Laboratory, Eskisehir, Turkey

[3]Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskisehir, Turkey

INTRODUCTION:

Tasimelteon (TAS), which was approved for treatment of non-24-hour sleep–wake disorder in 2014, is a selective agonist for the melatonin receptors MT1 and MT2 (1). The main purpose of the described study herein was to investigate optimum LC-MS/MS conditions to develop a selective, sensitive and validated analytical method for quantitative determination of TAS.

MATERIALS AND METHODS:

The experimental work was succeed using an LCMS-8040 series liquid chromatograph mass spectrometer. The LC part of the instrument (Nexera XR series from Shimadzu, Japan) was composed of two LC-20AD binary pumps with a three-way degasser (DGU-20A3R), an SIL-20AC autosampler, a CTO-10ASVP column oven, a CBM-20A communications bus module. Conventional reversed phase LC solvents and MS additives were used for method development applications.

RESULTS:

The separation of TAS was achieved using a second-generation monolithic silica column (Chromolith® High Resolution RP-18e, 100 × 4.6 mm from Merck KGaA). The mobile phase was a mixture of 0.1% (v/v) formic acid in water and 0.1% (v/v) formic acid in acetonitrile (60: 40 (v/v), pH=2.6). The flow rate was 0.5 mL/min. The mass spectrometer was operated at a mass range from m/z 100 to m/z 800 using an electrospray ionization in positive mode (ESI+). The MS conditions were optimized to drying gas (nitrogen) flow 15 L/min, nebulizing gas (nitrogen) flow 3.0 L/min, collision gas (argon), CDL temperature 250 °C and heat block temperature 450 °C. Multiple Reaction Monitoring (MRM) mode were used throughout all analysis.

CONCLUSIONS:

TAS is considered to be one of the promising insomnia drugs of the future; it is the first approved treatment in US for non-24-hour sleep–wake disorder (2). This is the first study, in which LC-MS/MS conditions were characterized for quantitative analysis of TAS.

ACKNOWLEDGEMENTS:

Authors would like to acknowledge Anadolu University Scientific Research Projects Commission for financial and technical support (Project No: 1606S567).

REFERENCES:

1. Dhillon S, Clarke M (2014). Drugs, 74(4):505-511.
2. Bonacci JM, Venci JV, Gandhi MA (2015). Journal of Pharmacy Practice, 28(5): 474-478.

P- 241: NEW APPLICATIONS OF SPECTROPHOTOMETRIC TECHNIQUES FOR THE SIMULTANEOUS DETERMINATION OF ZOFENOPRIL CALCIUM AND HYDROCHLOROTHIAZIDE IN PHARMACEUTICAL FORMULATIONS

[1,2] Lotfy, HM., [3] Tiris, G., [4] Erk, N.

[1]Cairo University, Faculty of Pharmacy, Analytical Chemistry Department, Cairo, Egypt

[2]Future University, Faculty of Pharmaceutical Science and Pharmaceutical Industries, Pharmaceutical Chemistry Department, Cairo, Egypt

[3]Bezmialem Vakif University Faculty of Pharmacy,Department of Analytical Chemistry, Istanbul, Turkey

4Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Combinations of zofenopril calcium (ZOF) and hydrochlorothiazide (HYD) are used for the treatment of arterial hypertension. Dosages values different from those presented on the label of pharmaceuticals can significantly impact a consumer's health (1-2).

Methods: Development and comparison of two different spectrophotometric techniques, one with absorbance subtraction and the other with ratio difference, were presented for simultaneous determination of ZOF and HYD , in pharmaceutical formulations.

RESULTS:

The zero order absorption spectra of the ZOF and HYD were recorded. The zero order spectra recorded of ZOF at 233.0 nm was measured. The absorbance factor (AF) was calculated as 2.87. The ratio difference spectrophotometric technique was applied for simultaneous determination of each drugs. The difference amplitudes in the ratio spectra at 241.0 – 288.9 nm and at 271.3 – 324.1 nm were selected to determine ZOF and HYD in the binary mixture. Linearity was found to be acceptable over the concentration ranges of 5-35 mu g mL(-1) and 3 -20 mu g mL(-1) for ZOF and HYD, respectively.

CONCLUSIONS:

Based on the exprimental results, the developed methods enables and simultaneous determination of ZOF and HYD in pharmaceutical dosage forms. The simplicity of the method allows its use in routine analysis for quality control.

REFERENCES

1. Parati G, Omboni Sand Malacco E (2006). Blood press, 15:7-17.
2. Pasini AF, Garbin U, Nava MC (2007). Am j hypertens, 20: 443-450.

P-242: RESOLUTION OF TWO-COMPONENT MIXTURE IN COMBINED DOSAGE FORMS CONTAINING PROTON PUMP INHIBITORS BY USING RATIO FIRST DERIVATIVE UV SPECTROPHOTOMETRY

[1] Erk, N. , [2] Bay, MS.

[1]Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

[2]Turkish Medicines and Medical Devices Agency, Department of Analysis and Control Laboratories, Ankara,Turke

INTRODUCTION:

Domperidone (DOM), 6-chloro-3-[1-[3-(2-oxo-3H-benzimidazol-1-yl)propyl]piperidin -4-yl]-1H-benzimidazol-2-one is a dopamine antagonist with antiemetic property similar to metoclopramide and neuroleptic drugs (1,2). Lansoprazole (LA), 2-[[3-methyl-4-(2,2,2-trifluoroethoxy)pyridin-2-yl] methylsulfinyl]-1H-benzimidazole is a proton pump inhibitors. There are many combinations of proton pump inhibitors with Domperidone and Lansoprazole, available in local markets.

METHODS:

First derivative UV and ratio derivative spectrophotometric methods are described for the simultaneous determination of benzimidazole proton pump inhibitor used for the treatment of gastrointestinal disorders. In the first derivative spectrophotometry with a zero-crossing technique of measurement is used for the cited drugs in binary mixtures without previous separation step. The other method, is based on ratio derivative spectrophotometry, the amplitudes in the first derivative of the ratio spectra were selected to determine DOM and LA in the binary mixture.

RESULTS:

The first derivative spectrophotometry, the signals in the first derivative UV spectra at 282.8 and 230.5 nm are selected to simultaneous determination DOM and LA in the binary mixture. The linear regression of derivative absorbance signals on concentration gave the equation; y= -0.047x – 0.0046 (R2: 0.9961) at 282.8 nm and y = -0.0028x - 0.0071 (R2 : 0.9997) at 230.5 nm for DOM and LA, respectively. The calibration curves were linear over the ranges of 8-20 µg mL-1 and 6 - 24 µg mL-1 for DOM and LA, respectively. The results of assay of DOM and LA are 100.4 ± 1.06 and 99.1 ± 1.25, respectively.

CONCLUSIONS:

The proposed methods, which gives thoroughly comparable data, are simple, fast, require no preliminary separation steps, can reliably be used for routine analysis of DOM and LA in bulk drug and laboratory prepared binary mixtures.

REFERENCES:

1. The Merck Index, An Encyclopedia of Chemicals, Drugs, and Biologicals (2001) Merck & Co, Inc,Whitehouse Station, NJ 2332:6306
2. Brogden RN, Carmine AA, Heel RC (1982). Drugs, 24:360

P-243: ELECTROCHEMICAL BEHAVIOURS OF ANTHISTAMINES; LEVOCETRIZINE AND DESLORATADINE IN AQUEOUS SOLUTIONS

[1,2] Bakirhan, NK. Ozturk, K., Uslu, B., Ozkan, SA.

[1]Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

[2]Hitit University, Faculty of Art&Science, Department of Chemistry, Corum, Turkey

INTRODUCTION:

Levosetirizine (LCZN) and Desloratadine (DESL) are used as antihistamines. In this study, it is aimed to investigate the electrochemical behavior of them in the direction of oxidation by using glassy carbon electrode (GCE) and modified forms with nanoparticles. In this way, it is planned to obtain information about the mechanisms. The main purpose of this study is examine in detail the mechanisms of drug substances and to use them to illuminate these mechanisms of oxidation /reduction reactions in drug metabolism in the human body.

MATERIALS AND METHODS:

Autolab 100N was used as electrochemical analyzer. Ag/AgCl electrode as reference, platin electrode as counter and modified GCEs were used as working electrodes. pH, supporting electrolyte and scanning speed parameters were investigated by cyclic, differential pulse voltammetry methods. The influence of the pH on the oxidation peak current of 5.0×10−5 M LCZN on β-cyclodextrin modified glassy carbon electrode (β-cyclodextrin/GCE) and 1.0×10−4 DESL on ZnO:MWCNT composite modified GCE (ZnO:MWCNT/GCE) were checked via phosphate (pH 2.0, 3.0 and 6.0, 7.0, 8.0), acetate (pH 3.5-4.5-5.5), Britton-Robinson (BR) (pH 2.0-11.0) buffers. Scan rate study was applied by cyclic voltammetry between 10 and 350 mV s−1.

RESULTS:

Shifts in potential, peak current, smoothness of peak shape are all considered; the optimum pH and buffer solution were determined as pH 2.0 and B-R buffer for LCZN and pH 5.5 and acetate buffer for DESL. LCZN gave a linear relationship on the oxidation peak current (Ip) with the scan rate (v) that showed predominantly adsorption control process. On the other hand, the results of the scan rate for DESL, the slope of the logv - logIp curve (~ 0.236) was less than the theoretical value of 0.5, which resulted in diffusion control of the electrode surface.

CONCLUSIONS:

Electrochemical behaviors of antihistamines LCZN and DESL were investigated in aqueous solutions. Redox reactions were investigated on developed electrodes.

ACKNOWLEDGEMENTS:

The authors acknowledge the financial support of Ankara University, Department of Scientific Research Project (Project Number:17L0237001).

P-245: COMPARISON OF SAMPLE PREPERATION TECNIQUES ON HUMAN BLOOD PLASMA FOR LC/MS METABOLOMIC STUDIES

Kaplan, O., Kocak, E., Celebier, M.

Hacettepe University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Although there are many sample preparation procedures for metabolomic studies in the literature, which method is superior to the other is still a question mark (1). In this study, four methods including ultrafiltration, methanol precipitation, solid phase extraction and solid liquid extraction were compared within each other and it was tried to find out which method performs better results for metabolite profiling.

MATERIALS AND METHODS:

In this work, 4 methods including ultrafiltration, methanol precipitation, solid phase extraction and solid liquid extraction were compared within each other. Metabolite extraction methods were applied individually on same plasma sample to evaluate the differences in a true way. For each method, the final plasma concentration kept equal and all samples were analyzed by LC/MS Q-TOF using a C-18 chromatographic column. The results and data mining were evaluated using the same statistical tests and methodologies and interpreted accordingly.

RESULTS:

The results were examined by XCMS (a R computer language-based metabolite profiling software). The method with the highest number of peaks was referred as the optimum method for sample preparation in human plasma samples. In addition, principal component analysis (PCA) results were compared within each other. According to these data, precipitation method with methanol gives maximum number of peaks with 624 peak counts, the ultrafiltration method is the second one with 444 peak counts, where the liquid extraction method and the solid phase extraction method are third and fourth, with 325 peak counts and 193 peak counts respectively. As term of peak count is peaks which have $p<0.05$ and $R>0.90$ values as statistically valid peaks.

CONCLUSIONS:

Metabolites do not have a universal sample preparation method because of their chemical and physical properties. In the present study, it was tried to indicate the optimum sample preparation technique for human blood plasma samples to identify maximum number of peaks in LC / MS Q-TOF based experiment.

REFERENCES:

1. Vuckovic D (2012). Analytical and bioanalytical chemistry, 403(6):1523-1548

P-246: ANALYTICAL METHOD DEVELOPMENT ON LIQUID CHROMATOGRAPHY/ MASS SPECTROMETRY (LC/MS Q-TOF) FOR METABOLOMIC STUDIES AT DIFFERENTIAL DIAGNOSIS OF ASCITES

Kaplan, O., Celebier, M., Suslu, I.

Hacettepe University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Pathological fluid collected in the peritoneal cavity is called ascitic fluid. The concept of the differential diagnosis of ascites is the process of diagnosing the disease that causes ascites formation. In this study, metabolomic studies were performed by liquid chromatography/mass spectrometry (LC/MS Q-TOF) to tell nonmalignant ascitic samples (Group C) and malignant ascitic samples (Group T) apart.

MATERIALS AND METHODS:

Study text consist of three main experimental parts: Analytical method development, metabolite profiling and targeted metabolomics. In the method development step, two different sample preparation methods, ultrafiltration and methanol precipitation, two different chromatography columns, HILIC and C18 columns, two different MS modes, positive and negative MS modes, were tried and compared within each other. XCMS and MetaboAnalyst were used for data mining process (1).

RESULTS:

Ultrafiltration technique, HILIC column and positive mode MS methods were determined as the method giving the maximum number of peaks and the study was performed under these optimum conditions. Metabolite profiling studies were carried out and 141 peaks were found as minimum two times differentiating between two groups. Six of these peaks were identified in targeted metabolomic studies and chemical structures were characterized.

CONCLUSIONS:

This study aimed to find the differences in metabolome level between T and C groups by using LC/MS method. Thus, ascites differential diagnosis was performed in metabolome level. The results showed that 141 peaks between the two groups were statistically reliable and significant in quantity. This situation suggests that there are differences in metabolome level in the ascites fluid resulting from different diseases and these differences can be determined by the method developed in the present study.

REFERENCES:

1. Dunn WB et al., (2011). Nature Protocols, 6(7):1060-1083.

P-247: DEVELOPMENT AND VALIDATION OF A HILIC METHOD FOR SIMULTANEOUS DETERMINATION OF CARBOPLATIN AND DECITABINE

[1] Esim, O., [2] Gumustas, M., [1] Hascicek, C., [3] Ozkan, SA.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

[2]Ankara University, Institute of Forensic Sciences, Department of Forensic Toxicology, Ankara,Turkey

[3]Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Carboplatin (CRB) is an anticancer drug which is widely used as first line chemotherapeuetic for treatment of ovarian cancer. The major problem with ovarian cancer treatment is acquired carboplatin resistance. The use of decitabine (DEC), which is a DNA methyltransferase inhibitor, combined with carboplatin is a new perspective for modulating carboplatin resistance. The aim of this study is to develop and validate a Hydrophilic Interaction Liquid Chromatography (HILIC) method for the selective and reliable simultaneous determination of CRB and DEC from their bulk and pharmaceutical dosage forms.

MATERIALS AND METHODS:

Agilent 1100 series LC system (Wilmington, DE, USA), equipped with a G1379A degasser, G1311A quaternary pump, G1313 auto injector and G1315B diode array detector (DAD) was used for method development and validation studies.

A Kinetex HILIC (150x4,6 mm, 2,6 µm, 100Ao) (Phenomenex, USA) analytical column was used as stationary phase. An isocratic mobile phase consisting of acetonitrile:5 mM ammonium acetate buffer (92:8) was selected. Both CRB and DEC was detected at 220 nm wavelength. In order to optimize the chromatographic conditions, effects of flow rate and column oven temperature were also investigated. The optimized HILIC method was validated according to the ICH guidelines (1) from the view point of linearity, accuracy, precision, limit of detection (LOD) and quantitation (LOQ), etc.

RESULTS:

As a result of optimization studies, separation of CRB and DEC performed by using 5 µL injection volume, 1 mL/min flow rate and 15◦C column oven temperature. The retention times were 3.7 min and 7.8 min for DEC and CRB, respectively. Developed method was found linear in the range between 1 and 100 µg.mL-1 with correlation coefficient of 0.9996 and 0.9994 for CRB and DEC, respectively. Accuracy of the method was demonstrated by the application of pharmaceutical formulations as real samples.

CONCLUSIONS:

A sensitive and rapid determination method which can be used for the simultaneous determination of CRB and DEC from their bulk and pharmaceutical dosage forms was developed.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-116S395)

REFERENCES:

1. ICH Harmanised Tripatite Guideline (2005). Validation Of Analytical Procedures: Text And Methodology Q2(R1).

P-248: QUANTITATIVE ANALYSIS OF A BINARY MIXTURE IN A PHARMACEUTICAL DOSAGE FORM BY CONTINUOUS WAVELET TRANSFORM TECHNIQUE

Ustundag, O., Dinc, E.

Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Wavelet transform (WT) has gained wide acceptance as a valuable tool for signal processing tasks, due to their wide range of applications (1).

MATERIALS AND METHODS:

In this context, a new signal processing approach, ratio spectra - continuous wavelet transform (RS-CWT) method was developed for the

simultaneous determination of irbesartan (IRB) and hydrochlorothiazide (HCT) in a pharmaceutical dosage form.

RESULTS:

The RS-CWT method was applied to the UV spectra of the IRB and HCT. After applying many wavelet functions, the family consisting of bior1.3 was found to be suitable for the quantitative determination of the mentioned drugs.

CONCLUSIONS:

After the name (RS-bior1.3-CWT) was given, the calibration equations were obtained by measuring the CWT-amplitudes at 235.9 nm for the IRB determination and at 262.8 nm for the HCT determination, respectively. The proposed methods were successfully applied to the analysis of the IRB-HCT in the pharmaceutical tablets.

REFERENCES:

1. Dinc E, Baleanu D (2003). Talanta, 59(4):707-717.
2. Dinc E, Baleanu D, Ustundag O (2003). Spectroscopic Letters, 36:341-355.
3. Daubechies (1992). Ten Lectures on Wavelets, Society for Industrial and Applied Mathematics, Philadelphia.
4. Walczak B (2000). Wavelets in Chemistry, Elsevier Press, Amsterdam.
5. Dinc E, Baleanu D (2007). Mathematical Methods in Engineering, Springer. The Netherlands

P-249: SIMULTANEOUS QUANTITATIVE RESOLUTION OF ACTIVE COMPOUNDS IN A TABLET DOSAGE FORM BY UPLC TECHNIQUE

Ustundag, O., Dinc, E.

Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

An ultra performance liquid chromatography (UPLC) method was developed for the analysis of active compounds in a tablet.

MATERIALS AND METHODS:

A rapid and sensitive chromatographic approach, ultra performance liquid chromatography (UPLC) method was developed for the simultaneous quantitative resolution anti-hypertensive compounds (hydrochlorothiazide and irbesartan) of a tablet dosage form. Ultra performance chromatographic analysis was performed on a UPLC system consisting of a Waters Acquity equipped with binary solvent delivery pump, an auto-sampler and photo diode array (PDA) detector.

RESULTS:

The chromatographic separation was carried out by using a Waters Acquity UPLCTM BEH C18 column (50 mm x 2.1 mm, 1.7 µm i.d.). Integration was automatically performed by computer using Acquity UPLC software. Detection responses were measured in terms of peak area.

CONCLUSIONS:.

In conclusion, UPLC method may be considered more specific than other approaches. The developed UPLC method can be applied with great success to the routine quality control of the tablets containing IRB and HCT.

REFERENCES:

1. Coudoré F et al., (2011). Chromatographia, 74:559–565.

P-250: INTERACTION STUDIES OF CARBIDOPA WITH FISH SPERM DOUBLE STRAIN DNA USING UV-SPECTROSCOPIC TECHNIQUE

Senel, P., Golcu, A.

Istanbul Technical University, Faculty of Arts and Sciences, Department of Chemistry, Istanbul, Turkey

INTRODUCTION:

Carbidopa (Lodosyn) is a drug given to people with Parkinson disease or Parkinson-like symptoms (e.g. shakiness, stiffness, difficulty moving) to reduce peripheral adverse effects of levodopa. It is known as an enzyme blocker. It works by preventing the breakdown of levodopa in the bloodstream. This allows more levodopa to enter the brain, where it can decrease Parkinson's symptoms.

MATERIALS AND METHODS:

Drugs interact with the double helix DNA in either covalent or noncovalent way. The non-covalent way includes three modes of binding; electrostatic effects, groove binding and intercalation, among which intercalation is the most important binding mode (1). Small molecules when bind to DNA through intercalation, can damage DNA in disease cells (2). Many techniques have been applied for investigation of the interaction of drugs with DNA. These include; molecular spectroscopy methods such as UV spectrophotometry , fluorescence , circular dichroism spectroscopy , dynamic viscosity measurements, and high-performance liquid chromatography (3).

RESULTS:

In this study, the molecular interactions between Carbidopa and fish sperm double strain DNA have been studied using UV–Vis spectrophotometry technique and the binding constant (Kb) of drug to DNA was determined.

CONCLUSIONS:

When the results of the absorption spectra of carbidopa in the absence and presence of DNA are examined, it is understood that upon increasing the ratio of the concentration of DNA to drug, the absorption bands of carbidopa exhibited hypochromism, with red shifts.

REFERENCES:

1. Shahabadi N, Kashanian S, Darabi F (2010). Europ. J. Med. Chem., 45(9):4239-4245.
2. Raman N, Sobha S, Mitu L (2013). J. Saudi Chem. Soc., 17(2):151-159.
3. Zhang G, Hu X, Pan J (2011). Spectrochimica Acta Part A, 78: 687-694.

P-251: ELECTROCHEMICAL INVESTIGATION OF DNA BINDING ON SULPIRIDE BY CYCLIC VOLTAMMETRY

Senel, P., Golcu, A.

Istanbul Technical University, Faculty of Arts and Sciences, Department of Chemistry, Istanbul, Turkey

INTRODUCTION:

Sulpiride is a substituted benzamide derivative drug and a selective dopamine D2 antagonist with antipsychotic and antidepressant activity. In contrast to most other neuroleptics which block both dopamine D1 and D2 receptors, Sulpiride is more selective and acts primarily as a dopamine D2 antagonist. It appears to lack effects on norepinephrine, acetylcholine, serotonin, histamine, or gamma-aminobutyric acid receptors (1).

MATERIALS AND METHODS:

The application of electrochemical methods to the study of organic and metallointeraction to DNA provides a useful complements to the previously used methods of investigation. Small molecules, which are not amenable to such methods or because of overlap of electronic transition with those of the DNA molecules, can be studied via voltammetric techniques. In addition, an electrochemical system can also serve as a versatile and illuminating model for gaining insight into the in vivo action in living cells (2).

RESULTS:

The electrochemical investigation of interaction of sulpiride with double strain DNA has been investigated by cyclic voltammetric studies on glassy carbon electrode at physiological pH and the binding constant (Kb) of drug to DNA was determined.

CONCLUSIONS:

Cyclic voltammetry based assay was developed for the assessment of the effect of the medium, substituents, potential scan rate and a number of scans on the voltammetric response of sulpiride-DNA couple.

REFERENCES:

1. https://www.drugbank.ca/
2. Ravikumar Naik TR, Bhojya Naik HS (2008). Int. J. Electrochem. Sci., 3:409-415.

P-253: DEVELOPMENT OF NEW MONOLITHIC POLYSACCHARIDE-BASED CHIRAL HPLC COLUMNS FOR ENANTIOMERIC SEPARATION

Ratih, Asmari, M., El Deeb, S.

Institute of Medicinal and Pharmaceutical Chemistry, TU Braunschweig, Germany

INTRODUCTION:

The planar polysaccharide, chondroitin sulfate A (CSA) and the maltodextrin (MD) which is a mixture of malto-oligo polysaccharide have been studied as potential chiral selectors. Through hydrolysis, MD is differentiated in various polymerization degrees known as dextrose equivalent (DE) values. CSA and MD have shown promising chiral recognition in capillary electrophoresis (CE). However, the enantiomeric separation using immobilized CSA and MD as chiral stationary phases (CSPs) in HPLC have not been reported. In this study, CSA and MD (DE 4-7) have been immobilized onto monolithic HPLC columns and tested as new polysaccharide-based CSPs. A CE method has been involved to figure out the enantiomeric recognition behaviour in the presence of chiral selector at certain concentrations.

MATERIALS AND METHODS:

Chromolith® Widepore 300 Epoxy 100-4.6 mm column and Chromolith® NH2 100-4.6 mm column were kindly provided by Merck KGaA Darmstadt, Germany. H_2SO_4, $NaIO_4$, $NaCNBH_3$, $NH_2CH_2CH_2NH_2$, Na_2HPO_4, CSA sodium salt (bovine trachea), MD (DE 4-7), (R, S)-amlodipine, and (R, S)-verapamil were acquired from Sigma-Aldrich (Steinheim, Germany). Acetonitrile (HPLC grade) were obtained from Merck (Darmstadt, Germany). Water was purified by Arium® Sartophore 0.2 µm, Sartorius (Gottingen, Germany).

CSA and MD were introduced by circulating them into monolithic epoxy and monolithic amine column under basic condition at a constant low flow rate, respectively. Afterward, the immobilization process was followed by a Schiff base reaction. The enantiomeric separations were performed using CE Agilent® and HPLC Hitachi®.

RESULTS:

The immobilized CSA-based and MD-based HPLC chiral columns have shown enantiomeric separations of amlodipine and verapamil as model compounds.

CONCLUSION:

The optimal concentrations of the chiral selectors which were obtained by CE method showed successful separations after immobilization on HPLC columns. Further studies will be conducted by experimental design for method optimization and by molecular modelling to investigate the possible interaction mechanisms between the two chiral selectors and target drugs.

ACKNOWLEDGEMENTS:

This study was supported by a research grant from Indonesia Endowment Fund for Education (LPDP), Ministry of Research, Technology-Directorate General of Higher Education (RISTEK DIKTI), Indonesia.

REFERENCES:

1. Zhao L et al., (2016). J. Chromatogr. A, 1446:125-133.
2. Nojavan S et al., (2014). Chirality, 26:394-399.
3. Guiochon G (2007). J. Chromatogr. A, 1168:101-168.
4. Chankvetadze B et al., (2003). Chem. Lett., 32:850–851.
5. Nishi H (1996). J. Chromatogr. A, 735:345-351.

P-254: DETERMINATION OF CIPROFLOXACIN IN AN OPHTHALMIC SOLUTION BY DERIVATIVE SPECTROPHOTOMETRIC METHOD

Dermis, S., Kilic, S., Ertekin, ZC., Dinc, E.

Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Ciprofloxacin is an antiinfective agent which belongs to the class of fluoroquinolones. Beside its systemic use, it is also indicated for the bacterial eye infections (1). The purpose of this study was to develop and validate a first derivative spectrophotometric method and its application to the analysis of ciprofloxacin eye drops.

MATERIALS AND METHODS:

The absorbance spectra of calibration samples were recorded between 200-400 nm in the linear working range of 3.0-28.0 µg/mL. Zero order and first derivative spectra of the calibration set were given in Figure 1. The calibration equation was obtained using the derivative values at 283.2 nm. The method was validated by means of recovery, standard addition and repeatability studies. After validation studies, the proposed method was applied for the analysis of eye drop solution which contained 3.5 mg/mL ciprofloxacin.

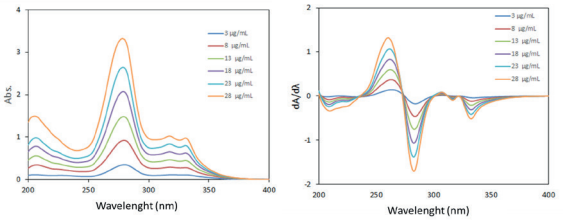


Figure 1. Zero order and first derivative spectra of calibration set

RESULTS:

The proposed method was proved to be accurate, precise, selective and reliable by the validation studies. The average of ten assay results were calculated as 3.47 mg/mL (s=0.03 mg/mL).

CONCLUSIONS:

A simple derivative spectrophotometric method was developed, validated and then it was applied to the determination of ciprofloxacin in eye drop formulations.

REFERENCES:

1. Adenis et al., (1996). European Journal of Ophthalmology, 6:368-374.

P-255: A COMPARATIVE STUDY ON THE LIQUID CHROMATOGRAPHIC RETENTION & SEPARATION CHARACTERISTICS OF SEVEN PARABEN DERIVATIVES IN DIFFERENT COLUMNS

[1,2] Ozcan, S., [1,2] Kozanli, M., [1,2] Can, NO.

[1]Anadolu University, , Faculty of Pharmacy, Department of Analytical Chemistry Eskisehir, Turkey

[2]Anadolu University, Faculty of Pharmacy, Doping and Narcotic Compounds Analysis Laboratory, Eskisehir, Turkey

INTRODUCTION:

Paraben derivatives are widely used as antimicrobial preservatives in foods, cosmetics and pharmaceuticals (1). Variations on the liquid chromatographic retention and separation of seven paraben derivatives, namely methylparaben (MP), ethylparaben (EP), n-propylparaben (NPP), i-propylparaben (IPP), n-butylparaben (NBP), i-butylparaben (IBP) and benzylparaben (BP) were studied by utilizing different types of stationary phases (n=3). The effect of particle structure, retention characteristics, system suitability parameters were investigated, and the results were compared with each other for a brief performance evaluation.

MATERIALS AND METHODS:

Analyses were performed using a Nexera series of UHPLC system, which was composed of the following components (all from Shimadzu, Japan): Two LC-30AD binary pumps equipped with a DGU-A5R on-line degasser for each, an SIL-30AC autosampler, a CBM-20A system controller and an

SPD-M20A photodiode array detector. Acceptable chromatographic separation was succeeded under gradient elution conditions without use of buffer, and compounds were monitored at 254 nm. The proposed method was applied on real cosmetics and pharmaceuticals samples.

RESULTS:

The highest separation efficiency with acceptable resolution and reasonable retention was obtained when Kinetex® C18 (2.6 µm particle size, 150 x 3.0 mm, Phenomenex Co.) column was used, which was followed by C18 BEH (1.7 µm, 50 × 2.1 mm, Waters) and Kinetex® C18 (1.3 µm particle size, 50 x 2.1 mm, Phenomenex Co.).

CONCLUSIONS:

Moderate differences in the system suitability results were observed regarding the examined columns, which were inferred to be associated to the differentiations in the particle size and pathway length. Among the columns tested, the best choice for separation of mentioned compounds seem to be Kinetex® C18 with 2.6 µm particles.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Anadolu University Scientific research Projects Commission (Project No: 1606S551).

REFERENCES:

1. Shen HY, Jiang HL, Mao HL, Pan G, Zhou L, Cao YF (2007). Journal of Separation Science, 30(1), 48-54.

P-256: DETECTION OF TYROSINE NITRATION WITH VOLTAMMETRIC TECHNIQUES

[1] Topkaya, SN., [2] Ozyurt, VH., [3] Cetin, AE., [2] Otles, S.

[1]Izmir Katip Celebi University, Faculty of Pharmacy, Department of Analytical Chemistry, Izmir, Turkey

[2]Ege University, Faculty of Engineering, Department of Food Engineering, Izmir, Turkey

[3]Dokuz Eylul University, Izmir International Biomedicine and Genome Institute, Izmir, Turkey

INTRODUCTION:

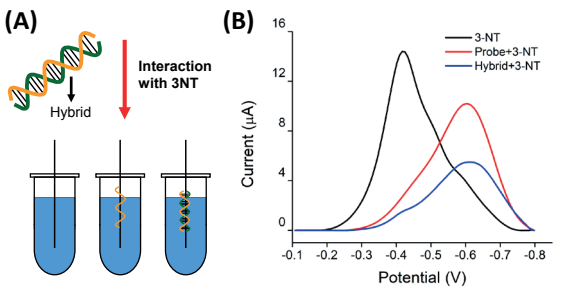
Nitrating agents act as reactive compounds and help formation of nitric oxide and peroxynitrit. They can react with a number of biomolecules such as DNA, proteins and lipids. Tyrosine nitration changes the key properties of amino acids such as redox potential, hydrophobicity and the values of pKa. They also react with Tyrosine (Tyr) to form 3- Nitro-L-tyrosine (3-NT) replacing by hydrogen in the ortho position of the phenolic ring of the Tyr residues with a nitro group (-NO2). Therefore, 3-NT could be used a marker of nitrative stress.

MATERIALS AND METHODS:

In this work, we aim to detect 3-NT and its interaction with DNA oligonucleotides by using its oxidation/ reduction properties with differential pulse voltammetry (DPV). In our platform, we activate electrodes to provide effective surface area, immobilize the probe sequences were onto the electrodes by dipping electrodes into the probe solution and we activate the probe coated electrodes with its target sequence to create hybrid form on the surface of electrodes (Figure A).

RESULTS:

In order to detect the hybridization and interaction events, we measured the changes in the oxidation signal of the guanine bases of DNA versus Ag/ AgCl reference electrode with DPV. 3-NT behaves as a 'hybridization indicator' due to its distinct electrochemical behavior to different strands of DNA. After interaction with 3-NT, guanine oxidation signals of probe signals decreased dramatically whereas hybrid signals remain almost unchanged. The signal differences enabled us to distinguish single stranded DNA (ssDNA-probe) and double stranded DNA (dsDNA-hybrid) without using a label or tag. We also, for the first time, showed the detection of hybridization of DNA by using the reduction signal of 3-NT. We observed the changes of the reduction signals of 3-NT after the interaction of probe and hybrid sequences (Figure B).



CONCLUSIONS

We demonstrated a new hybridization indicator, 3-NT, by utilizing both its reduction and guanine oxidation signal changes, where the total time of our measurements as short as 1hr., including activation of electrodes, hybridization, attachment of DNA oligonucleotides to the surface and interaction with 3-NT.

REFERENCES:

1. Topkaya et al., (2018). Biosensors and Bioelectronics, 102:464-469.

P-257: STABILITY-INDICATING UPLC METHOD FOR THE DETERMINATION OF MONTELUKAST SODIUM, DESLORATADINE AND THEIR IMPURITIES FROM FIXED DOSE COMBINATION TABLETS

[1,2] Zengin Kurnali, S., [1] Ozturk, C., [1] Uslu, A., [2] Uslu, B.

[1]Nobel Pharmaceutical Company, R&D Center, Düzce, Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Montelukast Sodium, a specific cystenyl leukotriene receptor antagonist belong to styryl quinolines and Desloratadine is a non-sedating H1 ant,-histamine. Fixed dose combination tablet containing Montelukast Sodium and Desloratadine used for the treatment of asthma and allergic rhinitis. UPLC refers to ultra-performance liquid chromatography, which enhance mainly in three areas: “speed, resolution and sensitivity. This new category of analytical separation science retains the practicality and principles of HPLC. In the last decade, Bilayer tablet technology interested in developing a combination of two or more Active Pharmaceutical Ingredients (API) in a single dosage form (bilayer tablet) has increased in the pharmaceutical industry, promoting patient convenience and compliance. Bilayer tablets can be a primary option to avoid chemical incompatibilities between API by physical separation. The aim of this study is to demonstrate an UPLC method for the simultaneous, determination of montelukast sodium, desloratadine and their impurities from fixed dose combination.

MATERIALS AND METHODS:

Waters Acquity UPLC H-Class system equipped with a diode array detector was used for analysis. Analyses have been conducted with the the Zorbax SB-PHENYL (50 mm x 4.6 mm, 1.8 µm), analytical column. The mobile phase consisted of acetonitrile with triflouroaceticacid: ammonium acetate buffer solution by flowing program at 25°C. Detection wavelength was selected as 238 nm. Forced degradation studies were carried out by using tablet form. The degradation studies were performed under certain conditions included acid hydrolysis, base hydrolysis, oxidation, fotostability, heating in the oven at 70°C. The results were compared to the untreated tablet solution.

Lorclast 5/10 mg Film Coated Tablets (Nobel Pharmaceutical Company) was used as a test product. These tablets are bilayer tablets. Montelukast sodium on one layer and desloratadine on the other layer are present as active ingredient. In addition, bilayer Lorclast 5/10 mg Film Coated tablets containing montelukast and desloratadine in different layers as well as monolayer tablets containing both in the same layer were also analyzed.

RESULTS:

Degradation studies were carried out to examine the selectivity of the analytical method. It was observed that the degradation products did not interfere with the active substances in 6 different degradation conditions. Therefore, the developed method is suitable for analysis of the active ingredients simultaneously with possible degradation product.

Bilayer tablets are lower in impurity degradation under ICH accelerated stability conditions (40°C ± 2°C/75% RH ± 5% RH) and the product is more stable.

CONCLUSIONS:

As a result of this study, fast, simple, sensitive, selective and fully validated UPLC method has been developed under developed conditions. The proposed rapid and sensitive UPLC method will be readily applicable in quality control laboratories since for simultaneous quantification of Montelukast Sodium and Desloratadine. Thus, the feasibility of the method in complex matrices such as drug samples has also been demonstrated.

P-258: DETERMINATION OF GRANISETRON IN PHARMACEUTICAL PREPARATIONS BY RRLC WITH FLUORESCENCE DETECTION

[1] Ozyurek, B., [1] Cecen, SD., [2] Dal AG.

[1]Anadolu University, Graduate School of Health Sciences, Eskisehir, Turkey

[2]Anadolu University, Department of Analytical Chemistry, Eskisehir, Turkey

INTRODUCTION:

Granisetron (GRA) is a selective 5-hydroxytryptamine receptor antagonist that has proved to be effective in the prevention and treatment of chemotherapy-induced nausea and vomiting following intravenous administration (1). In this study a rapid, sensitive and specific liquid chromatographic (RRLC) method was developed, validated and applied to pharmaceutical preparations of GRA.

MATERIALS AND METHODS:

The instrument was Agilent Technologies 1200 LC series with RF detection. All chemical solutions were analytical grade. GRA was dissolved in MilliQ water. Metoprolol was used as an IS. The excitation and emission wavelengths were 223 nm and 340 nm, respectively. Separation was achieved by a C6 phenyl column (3.0×150.0 mm, 5.0 µm i.d.). 30 mM acetate buffer:methanol (7:3, v/v) (pH 4.0) system was used as a mobile phase at a flow rate of 0.85 mL/min.

RESULTS:

For the optimization of method, buffer concentration, organic solvent ratio, pH, flow rate and injection volume were investigated. Retention times for GRA and IS were 4.57 min 2.95 min, respectively under the optimum conditions. The validation of the developed method was examined by linearity, precision, accuracy, sensitivity, stability, specificity and robustness parameters. The LOQ of the method was found to be 2.04×10-8 M. The developed method was successfully applied to GRA tablets and ampoules.

CONCLUSIONS:

The method described here is simple, fast, sensitive and reproducible. It was applied to tablets containing 1 mg GRA and ampoules containing 3 mg/mL GRA. The contents of the pharmaceutical preparations were found to be in the limits of USP39 (2). This method is proposed for the routine analysis of GRA.

ACKNOWLEDGEMENTS:

This study was supported by Anadolu University Scientific Research Projects Commission under the grant no: 1505S428.

REFERENCES:

1. Hewala I et al., (2010). Talanta, 82(1):184-195.
2. U.S. Pharmacopeia National Formulation 39 (2016). The National Formulary 34, Rockville: United States Pharmacopeial Convention.

P-259: SPECTROPHOTOMETRIC AND POTENTIOMETRIC DETERMINATION OF ACID DISSOCIATION CONSTANT (PKA) VALUES OF SOME NONSTEROİDAL ANTİ-INFLAMMATORY DERIVATIVES OF 3-SUBSTITUTED PIPERAZINOMETHYL BENZOXAZOLINONES

[1] Altunterim, S., [2] Nalbur, AM., [2] Guzeldag, HB., [2] Durmaz, NA., [2] Hekimoglu, HE., [3] Baymak, MS., [4] Palaska, E., [1,2] Celik, H.

[1]Near East University, Department of Analytical Chemistry, Nicosia, TRNC

[2]Yeditepe University, Department of Analytical Chemistry, Istanbul, Turkey

[3]Marmara University, Department of Chemistry, Istanbul, Turkey

4Hacettepe University, Department of Pharmaceutical Chemistry, Ankara, Turkey

INTRODUCTION:

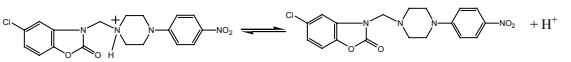
Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most widely used medications in the world due to their demonstrated efficacy in reducing pain and inflammation (1). NSAIDs have a crucial role in management and treatment of many diseases and disorders as headaches, dental pain management, osteoarthritis, rheumatoid arthritis, dysmenorrheal, ankylosing spondylitis and gout (2). In this study, we aim first to determine the pKa values of twenty 3-(4-substituted piperazinomethyl) benzoxazolinone derivatives (HH01-20) using spectrophotometric methods. Potentiometry is used later to confirm acidity constants obtained. The relevance of this study lays in the importance of determining the acidity constant of the studied compounds thus to further understand their chemical characteristics and other pharmacological effects (3). Furthermore, we also discuss the relationship between the acidity constant and analgesic/anti-inflammatory activities of these drug candidates.

MATERIALS AND METHODS:

In this study, the pKa values of twenty compounds have been investigated by using Agilent 8453 UV-Vis spectrophotometer. The concentration of the stock solutions of all studied compounds was 0.01 M in acetonitrile. The final concentration in the buffer solution was 2x10-5 M. Simple buffer systems were used with pH values between 1 and 12 and the chemicals used to prepare these buffer solutions were of analytical grade. In the potentiometric method, Metter Toledo pH 2100 Series was used.

RESULTS:

To understand the chemical interaction between the compounds and their pharmacological effects, the acidity constant (Ka) is a considerable important parameter. The link between Ka and the compound is used as a part of the investigations of new synthesis method for a drug candidate and in the explanation of the biopharmaceutics properties of these substances. The position of the equilibrium reaction was suggested based on the experimental evidence for studied compounds. The pKa values of these compounds were determined to be between 7.36 and 8.99. In view of the experimental confirmation, the equilibrium between protonated and unprotonated form can be given as follows:



It was suggested that the protonation b should b be on the nitrogen atom of piperazine ring. Analgesic activities of molecules were compared with pKa values of molecules. Due to the acidic and / or basic character of the compounds that show different activities, the ionization degrees of them could be determined by pH values and acidity constant with regarding its medium.

Conclusion: Our results suggest that analgesic/anti-inflammatory activities of HH01-20 changed when the pKa values of compounds were changed. Based on the experimental data, the electron withdrawing groups

(chlorine or fluorine atom) on benzoyl derivatives at the 6th position of benzoxazolinone or on the main structure of benzoxazolinone ring showed more basic character. Acetyl substituted derivatives have shown more basic characters than the other compounds and have given more pharmacologic activities.

REFERENCES:

1. Laine L (2001). Gastroenterology, 120(3):594-606.
2. Zochling J, van der Heijde D, Dougados M, Braun J (2006). Annals of the Rheumatic Diseases, 65(4): 423-432.

P-260: AN ELECTROCHEMICAL SENSOR FOR SENSITIVE DETECTION OF KETOCONAZOLE BASED ON SEPIOLITE CLAY ELECTRODE

[1] Aydar, S. [2] Yazan, Z.

[1]Istanbul University, Faculty of Engineering, Department of Chemistry, İstanbul, Turkey

[2]Ankara University, Faculty of Science, Department of Chemistry, Ankara, Turkey

INTRODUCTION:

Ketoconazole, cis-1-acetyl-4-{4-[2-(2,4-dichlorophenyl)2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy}piperazine (KC), is a highly effective broad spectrum antifungal agent (1). KC is one of the most famous antifungal medications and a potent inhibitor against the enzyme cytochrome P450. Several statins, including simvastatin and lovastatin, interact with this hepatic microsomal enzyme, which is responsible for a significant portion of the statin clearance (2). It suppresses testosterone and cortisol synthesis. KC has a strong antifungal activity against dermatophytes and yeast. KC containing shampoo rapidly exfoliates and pruritus, which is associated with pityriasis versicolor, seborrheic dermatitis and pityriasis capitis (3).

MATERIALS AND METHODS:

The method is based on a carbon paste electrode modified by the addition of sepiolite clay. Square wave adsorptive stripping voltammetry (AdsSWV) technique was employed with the electrode as the anode. Electrochemical redox properties of KC were investigated by using cyclic voltammetry (CV) on the same electrode.

RESULTS:

The CV studies show that KC has one oxidation signal at about +0.580 V in pH: 9.0 0.1M BR buffer. The anodic peak current of KC in AdsSWV varies linearly with the concentration range of 0.1 – 10 nmol L-1. Dedection limits and quantification limits were calculated as 0.025 nmol L-1 and 0.08 nmol L-1, respectively.

CONCLUSIONS:

This voltammetric technique has been applied to KC analysis in cosmetic preparation (ketoral shampoo) and acceptable results were obtained.

REFERENCES

1. Shamsipur M, Farhadi K (2000). Analyst,125: 1639–1643.
2. Gowda BG et. al., (2014). Der Pharma Chemica, 6 (5): 256-264.
3. El Ries MA et. al., (2013). Bulletin of Faculty of Pharmacy, 51: 49–55.

P-261: A NOVEL DNA NANOBIOSENSOR BASED ON GRAPHENE OXIDE DECORATED WITH GOLD NANOPARTICLES FOR THE DETECTION OF DNA INTERACTION WITH ANTICANCER DRUG

[1,2] Shahzad, S., [2] Kurbanoglu, S., [2,3] Karadurmus, L., [1] Shah, A., [2] Ozkan, SA.

[1]Quaid-i-Azam University, Department of Chemistry, Islamabad, Pakistan

[2]Ankara University, Department of Analytical Chemistry, Ankara, Turkey

[3]Adiyaman University, Department of Analytical Chemistry, Adiyaman

INTRODUCTION:

Cancer is the second leading cause of death after heart attack. Biosensors application holds great potential in cancer detection and clinical diagnosis. Electrochemical biosensors are most preferred in this regard owing to their small size, and ease of use, portability and cost effectiveness. This work is focused on improving the sensitivity of a nanobiosensor by modifying a screen-printed electrode with gold nanoparticles (AuNPs) and graphene oxide (GO) to detect interaction of anticancer drug Daunorubicin hydrochloride with DNA.

MATERIALS AND METHODS:

10 µL GO was dropped on electrode surface and allowed to dry at room temperature followed by placement of 5 µL AuNPs and 15 µL ct-dsDNA on screen printed electrode surface. All experiments were done in phosphate buffer of pH 4.65. Scanning electron microscopy (SEM) and UV-Visible spectroscopy were done to support drug-DNA interaction.

RESULTS:

Nanobiosensor developed with modification techniques implied an enhanced sensitivity of electrode in terms of surface area and the active sites that must increase on the electrode. By immobilizing nanoparticles and GO, the electrode surface became rich in active sites and thus the active area

(1). Physically it can be seen from SEM Images of electrode before and after modification with clear demarcation of granule like appearance of electrode after modification. Spectroscopic results supported these electrochemical results (2).

CONCLUSION:

A highly sensitive novel DNA electrochemical nanobiosensor was successfully developed for anticancer drug detection.

ACKNOWLEDGEMENTS:

This study was supported by TUBITAK – 2216 programme.

REFERENCES:

1. Bielawski CW, Dreyer DR, Park S, Ruoff RS (2010). Chem. Soc. Rev., 39:228-40.
2. Sarwar T, Husain MA, Rehman SU, Ishqi HM, Tabish M (2015). Molecular BioSystems, 11:522-31.

P-262: COMPARISON BETWEEN LIQUID CHROMATOGRAPHY AND RATIO DERIVATIVE SPECTROPHOTOMETRY FOR THE SIMULTANEOUS DETERMINATION OF PERINDOPRIL, INDAPAMIDE, AND AMLODIPINE TERNARY MIXTURES

[1,3] Karadurmus, L., [2] Gumustas, M., [3] Kurbanoglu, S., [3] Uslu, B., [3] Ozkan, SA.

[1]Adiyaman University, Faculty of Pharmacy, Department of Analytical Chemistry, Adıyaman, Turkey

[2]Ankara University, Institute of Forensic Sciences, Department of Forensic Toxicology, Ankara, Turkey

[3]Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Perindopril (PER) is an angiotensin converting enzyme (ACE) inhibitor used either alone or in combination in the treatment of hypertension. Indapamide (IND) is a benzamide-sulfonamide-indole derived diuretic and antihypertensive drug. Amlodipine (AML) is a member of the drug class long-acting dihydropyridine calcium channel blocker used to treat of hypertension and angina pectoris. Combination of Perindopril/ Indapamide/Amlodipine used for the treatment of arterial hypertension.

MATERIALS AND METHODS:

There exists no literature for the simultaneous detection of these ternary mixture using liquid chromatography with using new generation core-shell silica columns and ratio derivative spectrophotometry. Proposed study aimed to develop environmentally friendly, rapid, more sensitive and selective method for the simultaneous determination of PER, IND and AML using new generation HPLC columns. On the other hand, accuracy and precision of the developed liquid chromatography method and the ratio derivative spectrophotometry were compared by the help of student-t and F tests (1).

RESULTS:

In chromatographic separations, several mobile phase compositions were tested for the efficient separation, with using a new column technology related with superficially porous particles. Optimum chromatographic separation was achieved using a Kinetex C18 (150 x 4.6 mm I.D.5 µm) column at a flow rate of 1.5 mL min-1. The separation was carried out at 30 ºC and the diode array detector adjusted to 215 nm. As a comparison, a spectrophotometric method depends on the first derivative of the ratio spectra was developed. This method was based on a division of the absorption spectrum of the ternary mixture by a standard spectrum of the binary mixture of the components and then calculating the first derivative of the ratio spectrum.

CONCLUSIONS:

Finally, proposed methods were successfully applied for the simultaneous assay of the drug combination in pharmaceutical dosage forms with high recoveries.

REFERENCES:

1. Gumustas M, Kurbanoglu S, Uslu B, Ozkan SA (2013). Chromatographia, 76(21-22):1365-1427.

P-264: SYNTHESIS, CHARACTERIZATION, SPECTROSCOPIC STUDIES AND ANTIMICROBIAL ACTIVITY OF NEW SCHIFF BASES DERIVED FROM SALICYLALDEHYDES

Tuna Yildirim, S.

Erzincan University, Faculty of Pharmacy, Department of Analytical Chemistry, Erzincan, Turkey

INTRODUCTION:

Schiff base compounds which are synthesized from the amine and aldehyde (ketone), can interact with most of the metal ions to produce various complexes. Schiff bases are very important materials, these are widely used in medicinal chemistry due to their diverse biological, pharmacological, antitumor activities. These are also used as optical and electro sensors, in various chromatographic methods, to enhance selectivity and sensitivity. Schiff bases have gained much importance in biomimetic modelling applications, designing molecular magnet molecules and in liquid crystals aspect. Heterocyclic scaffolds containing an azole ring system and phenol derivatives have been known to possess a wide range of biological application such as antifungal, antimicrobial and antipyretic applications. Generally, these are excellent chelating agents, also used as catalysts, intermediates in organic synthesis, dyes,

pigments, polymer stabilizers.

MATERIALS AND METHODS:

In this study, the ligand of 5-hydroxysalicylidene-4-chloro-o-aminophenol was synthesized by the reaction of 5-hydroxysalicylaldehyde and 4-chloro-o-aminophenol in the absolute ethanol at 60 oC by the catalyzed of p-toluenesulfonic acid. Later, the complexes of this ligand were prepared with Co(II), Ni(II), Cu(II) and Zn(II) in acetate forms in pure EtOH. Than compounds characterized by spectroscopic techniques.

RESULTS:

All of the Schiff bases were found to be bidentate ligands involving the imino nitrogen and phenolic oxygen atoms in the complexes and M:L ratio were found to be 1:2 for all the complexes. The structures of ligands and complexes were identified using Elemental Analysis, FT-IR, 1H-NMR, 13C-NMR, UV-Vis, Magnetic Susceptibility, SEM, X-Ray and Thermogravimetric Analysis as techniques. After characterization, these Schiff bases were investigated for their biological activity and antimicrobial activity.

CONCLUSIONS:

One Schiff base ligand and six metal complexes were synthesized and the structures of ligands and complexes were characterized by various techniques and ensured the formation of compounds. Results of biological activities reveal that some of these compounds have good potential to be used in drug development.

ACKNOWLEDGEMENTS:

This study was supported by a grant of EÜBAP FEN-A-200314-0067

REFERENCES:

1. Abo Aly MM, Salem AM, Sayed MA, Abdel A (2015). Spectroch. Acta Part A: Molecular and Biomolecular Spectroscopy, 136:993–1000.
2. Emad Y, Ahmed M, Khulood S, Nadia S, Bashar A (2017). Arabian J. of Chemistry, 10:1639–164.
3. Adamantia K, Giannis SP, Catherine P, (2009). Polyhedron, 28: 3279-3283.

P-265: SYNTHESIS, SPECTROSCOPIC CHARACTERIZATION AND BIOLOGICAL ACTIVITIES OF SCHIFF BASES AND THEIR METAL (II) COMPLEXES

Tuna Yildirim, S.

Erzincan University, Faculty of Pharmacy, Department of Analytical Chemistry, Erzincan, Turkey

INTRODUCTION:

Compounds containing the –C=N (azomethine group) structure are known as Schiff bases, usually synthesized from the condensation of primary amines and active carbonyl groups. Schiff bases are considered as a very important class of organic compounds, having wide ranges of applications, such as a reagent of analysis. Schiff's bases considered as an important class of compounds in both the medical and pharmaceutical fields. Schiff bases are especially studied due to their synthetic flexibility, selectivity and sensitivity towards transition metals. Schiff base metal complexes have a variety of biological applications in clinical, pharmacological areas and several derivatives have been used as drugs. Schiff base Heterocyclic containing nitrogen, oxygen and sulfur atoms constitute a class of compounds which shows momentous biological activities, such as antiviral activity, antifungal, antioxidant, anti-malarial, anti-proliferative, anti-inflammatory, antitumor, anticancer, antibacterial activities, and antipyretic applications. They have important physiological activity and applications in analytical chemistry.

MATERIALS AND METHODS:

In this study, the ligand of 3-metoxy-5-nitrosalicylidene-4-chloro-o-aminophenol was synthesized by the reaction of 3-metoxy-5-nitrosalicylaldehyde and 4-chloro-o-aminophenol in the absolute ethanol at 60 oC by the catalyzed of p-toluenesulfonic acid. Later, the complexes of this ligand were prepared with Co(II), Ni(II), Cu(II) and Zn(II) in acetate forms in pure EtOH. Than compounds characterized by spectroscopic techniques.

RESULTS:

All of the Schiff bases were found to be bidentate ligands involving the imino nitrogen and phenolic oxygen atoms in the complexes and M:L ratio were found to be 1:2 for all the complexes. The structures of ligands and complexes were identified using Elemental Analysis, FT-IR, 1H-NMR, 13C-NMR, UV-Vis, Magnetic Susceptibility, SEM, X-Ray and Thermogravimetric Analysis as techniques. After characterization, these Schiff bases were investigated for their biological activity.

CONCLUSIONS:

One Schiff base ligand and six metal complexes were synthesized and the structures of ligands and complexes were characterized by various techniques and ensured the formation of compounds. Results of biological activities reveal that some of these compounds have good potential to be used in drug development.

ACKNOWLEDGEMENTS:

This study was supported by a grant of EÜBAP FEN-A-200314-0067.

REFERENCES:

1. Vigato PA, Tamburini S (2004). Coord. Chem.

Rev., 248:1717.
2. Abdur R et al., (2017). Journal of Molecular Str., 1145:132-140.
3. Mounira M, Tahar D, Farida S, Soraya B (2018). Journal of Molecular Str.,1151: 41-48.

P-266: METABOLOMIC PROFILING OF THE MOUSE PLASMA IN AIRWAY INFLAMMATION BY A GC-MS

[1] Recber, T., [2] Abohalaka, R., [1] Nemutlu, E., [2] Bozkurt, ET., [1] Kir, S., [2] Sahin Erdemli, İ.

[1]Hacettepe University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

[2]Hacettepe University, Faculty of Pharmacy, Department of Pharmacology, Ankara, Turkey

INTRODUCTION:

In metabolomics, the purpose is to identify and quantify as much as metabolites in a living organism. Metabolomic is very sensitive to a variety of external stimuli, drug exposures, genetic modifications, and disease pathways. Therefore metabolomics can help identifying the phenotype/pathophysiology of diseases and finding new therapeutic targets. Combined gas chromatography with mass spectrometry (GC/MS) is one of the most powerful techniques and commonly used in metabolomics studies.

Airway inflammation is an important component of various airway diseases such as asthma and chronic obstructive pulmonary disease (COPD). Identifying the possible changes in the plasma metabolomic profile in airway inflammation can help to find new biomarkers and therapeutic targets in these diseases. Therefore in the present study we aimed to investigate the systemic effect of airway inflammation in metabolomic profile of mouse plasma.

MATERIALS AND METHODS:

Lipopolysaccharide (LPS) was used in order to induce experimental airway inflammation. For this purpose, LPS was applied intranasally (60 µL; 0.1 mg/mL in PBS) to mice. The control group received vehicle (60 µL PBS) by the same route. 48 hours after LPS/ vehicle application mice were sacrificed by cervical dislocation, and the blood was collected by cardiac puncture.

Metabolomic profiling of plasma samples were performed using GC-MS (Shimadzu). The derivatized sample was injected split (1:10) by an auto sampler into a gas chromatograph equipped with a 30 m (+10 m duraguard)×0.25 mm i.d. fused-silica capillary column with a chemically bonded 0.25-µm DB-5MS stationary phase. The column temperature was held at 60°C for 1 min, then increased to 325°C, and held there for 10 min.

RESULTS:

Comparative metabolomic analysis of plasma samples from mouse was carried out based on the GC-MS metabolomic profiling to scan wide range of metabolites. The plasma samples were compared with control group in order to identified metabolites in a biological system. Urea, linoleic acid and L-alanine levels were significantly ($p<0.05$) altered in the LPS group.

CONCLUSIONS:

The altered level of alanine may indicate the oxidative stress, but interestingly not in the lactic acid level. The urea and linoleic acid levels were indicating changing in urea cycle and fatty acid metabolism.

ACKNOWLEDGEMENT:

Hacettepe University Scientific Research Projects Coordination Unit, Project No: THD-2017-16101

P-267: METABOLIC INFRASTRUCTURE OF PREGNANT WOMEN WITH METHYLENETETRAHYDROFOLATE REDUCTASE POLYMORPHISMS; METABOLOMIC ANALYSIS

[1] Recber, T., [2] Orgul, G., [2] Aydin, E., [2] Tanacan, A., [1] Nemutlu, E., [1] Kir, S., [2] Beksas, MS.

[1]Hacettepe University, Faculty of Pharmacy Department of Analytical Chemistry, Ankara, Turkey

[2]Hacettepe University, Faculty of Medicine, Department of Obstetrics and Gynecology, Ankara, Turkey

INTRODUCTION:

Today's innovative technologies permit comprehensive screening of the genome, transcriptome, proteome, and metabolome. In metabolomics, the purpose is to identify and quantify as much as metabolites in a biological system. Combined gas chromatography with mass spectrometry (GC/MS) is one of the most powerful techniques and commonly used in metabolomics studies. In this study, metabolomics analyzes were performed in maternal plasma by GC-MS to determine the metabolites to be used in the differentiation of pregnant women with methylenetetrahydrofolate reductase polymorphisms (MTHFR).

MATERIALS AND METHODS:

This study was consisted of 11 pregnancies with MTHFR polymorphisms as a study group and 10 normal pregnancies as a control group. Study group enrolls MTHFR C677T homozygosity, compound heterozygosity (C677T and A1298C) and MTHFR C677T heterozygosity in 3, 3 and 2 cases respectively.

The plasma sample was by centrifugation for 20 min at 1500 rpm at +4°C temperature. 100 µL of plasma was extracted with 900 µL methanol:water (8:1, v/v).

After extraction, 300 µL of the extract was evaporated to dryness in a vacuum dryer concentrator. Then, 20 µL of methoxyamine hydrochloride (20 mg mL-1) solution in pyridine was added to the sample for methoxymation. After 90 min at 30 °C, the sample were took out and derivatized with trimethylsilyl for 30 min at 37 °C by adding 80 µL of MSTFA with 1% TMCS. After derivatization, 50 µL of the samples were transferred into GC-MS vials.

RESULTS:

21 plasma samples were collected from pregnancies with MTHFR polymorphisms and healthy pregnant women. The data from GC-MS analysis is transformed into meaningful data through multivariate analysis of global profiling by PLS-DA allowing deeply investigation of the metabolomic profile differences between the groups. The PLS-DA scores plots demonstrate that genetic polymorphisms and gestational age caused changes in the metabolomics profile.

CONCLUSIONS:

The pre-existing differences determined by the genetic polymorphisms of the pregnancies were less marked than the effects of the gestational age. This is indicated that MTHFR polymorphic pregnant are more susceptible / sensitive to the gestational age.

REFERENCES:

1. Nurk E et al., (2004). The American journal of medicine, 1:26-31.
2. Nemutlu E et al., (2012). Physiol Genomics, 44.
3. Nemutlu E et al., (2012). Croatian Medical Journal, 53.

P-268: VOLTAMMETRIC DETERMINATION OF MERCURY USING A PENCIL GRAPHITE ELECTRODE

[1] Capan, T., [2] Arslan, H.

[1]Gazi University, Institute of Sciences, Department of Chemistry, Ankara, Turkey

[2]Gazi University, Faculty of Sciences, Department of Chemistry, Ankara, Turkey

INTRODUCTION:

Mercury is one of the most well-known toxic contaminants in aquatic ecosystems and even low-level Hg(II) exposure is considered to be a significant human health hazard. Because accumulation of Hg(II) through the food chain in the human body can lead to serious problems to the central nervous system and damage to the brain, kidney, lungs, and the developing fetus (1). Many analytical methods of mercury determination are also used. Of them; atomic absorption spectroscopy, inductively coupled plasma-mass spectrometry, spectrophotometry and voltammetry are the most common methods.

MATERIALS AND METHODS:

CHI 1230B model electrochemical analyzer was used in this study. The three electrode system consisting of a pencil graphite electrode as the working electrode, a platinum electrode as the counter electrode and Ag / AgCl (3M NaCl) as the reference electrode were used. The solutions used in the experiment were prepared using deionized water from the analytical purity salts of the respective chemicals. Optimal supporting electrode, optimum working electrode and working potential were determined. The interference effects of some ions in the Hg2+ assay were studied. The synthetic Hg2+ samples were then prepared. The synthetic samples were determined by Hg2+ standard addition method using square wave voltammetry.

RESULTS:

When studying the best working conditions for the determination of Hg2+, it was seen that the best working electrode was the pencil graphite electrode, the best supporting electrolyte was pH =7.0 phosphate buffer, and the working potential range was -1.20 to +0.60 V. In those conditions, it was observed of Hg2+ had a very low cathodic peak at -0,097 V and a well observed oxidation peak at +0,223 V in the cyclic voltammetry and square wave voltamograms. Hg2+ was determined using a +0,223 V anodic peak. It was observed that the detection limit of the work was 1.961×10-7 M and the limit of the quantity was 5.882×10-7 M.

CONCLUSIONS:

Electrochemical methods are more advantageous because they are faster and less costly than other methods. This study does not require any preliminary work with the reason that pencil graphite electrode is used as working electrode.

REFERENCES:

1. El-Safty, S.A,. Shenashen, M.A., (2012), Trends Anal. Chem. 38: 98–115.

P-269: PREPARATION OF A NEW MODIFIED CARBON PASTE ELECTRODE FOR ADRENALINE DETERMINATION

[1] Capan, T., [2] Uzun, D., [2] Hasanoglu Ozkan, E., [2] Sari, N., [2] Arslan, F., [2] Arslan, H.

[1]Gazi University, Institute of Sciences, Department of Chemistry, Ankara, Turkey

[2]Gazi University, Faculty of Sciences, Department of Chemistry, Ankara, Turkey

INTRODUCTION:

Adrenaline, also known as epinephrine [1-(3,4-dihydroxyphenol)-2-ethylaminoethanol], is found in body fluids and nerve tissues. Adrenaline is an important catecholamine that is secreted in response

to internal and external stressors and functions in the central nervous system of the mammals and acts as a hormone. Adrenaline increases digestion of glycogen, especially in the striated muscle, and reduces glycogen biosynthesis. It is effective on the heartbeat. In emergency situations, adrenalin can increase the heart rate and activate the whole organism. It is frequently used in emergency clinics, especially during a heart attack (1,2). Because of these reasons, determine of adrenaline is important. In this study, a novel modified carbon paste electrode using the Tryptophan-attached nanomaterial (4-Formyl-3-methoxyphenoxymethyl)-polystyrene (AMEBA-Trp) for determination of adrenaline was prepared. For this purpose, firstly, these compounds were synthesized. Then the optimal working conditions of the modified carbon paste electrode were determined.

MATERIALS AND METHODS:

Tryptophan-attached nanomaterial(AMEBA-Trp) was synthesized. Modified carbon paste electrode was prepared by mixing graphite powder, nujol and nanomaterial. Electric contacts were made by platinum wire. The electrochemical studies were carried out using an CHI 1230B electrochemical analyzer. The working electrode was a carbon paste electrode. The auxiliary and reference electrodes were a Pt wire and Ag/AgCl electrode, respectively. The determination of adrenaline is based on the oxidation of adrenaline by using square wave voltammetry with modified electrode.

RESULTS:

When studying the best working conditions for the determination of adrenaline, it was seen the best supporting electrolyte was pH =6.5 phosphate buffer. The oxidation peak at of adrenaline was observed +0,188 V by using square wave voltammetry. Determination of adrenaline was determined using a +0,188 V anodic peak of adrenaline. It was observed that the detection limit 8.6067×10-7 M and the limit of the quantity was 2.4938×10-6 M for adrenaline determination.

CONCLUSIONS:

The modified carbon paste electrode was found to be sensitive to adrenaline. With the prepared electrode, adrenaline can be determined in various samples.

REFERENCES:

1. Felix FS, Yamashita M, Angnes L (2006). Biosens. Bioelectron, 21(12): 2283-2289.
2. Shakrokhian S, Ghalkhani M, Amini MK (2009). Sensors and Actuators B: Chem.,137(2): 669-675.

P-270: DETERMINATION AND VALIDATION OF SILODOSIN IN PURE AND PHARMACEUTİCAL DOSAGE FORMS VIA HPLC-UV

[1] Akman, CT., [2] Atila, A., [2] Senol, O., [2] Yaman, E., [2] Kadioglu, Y.

[1]Erzincan University, Faculty of Pharmacy, Department of Analytical Chemistry, Erzincan, Turkey

[2]Atatürk University, Faculty of Pharmacy, Department of Analytical Chemistry, Erzurum, Turkey

INTRODUCTION:

Benign prostatic hyperplasia (BPH); is one of the most common diseases affecting the quality of life for elderly men, resulting in prostate enlargement due to proliferation of epithelial and smooth muscle cells in the lower urinary tract symptoms (LUTH) and the prostatic transition zone(1). Chemically (1- (3-hydroxypropyl) -5 - [(2R) -2- (2- (2,2,2-trifluoroethoxy) phenoxy] ethylamino) propyl] -2,3- indole-7-carboxamide), 'silodosin' is an α-1-adrenoceptor antagonist with high urogenic activity that does not affect other tissues used in the symptomatic treatment of BPH. alpha-1-adrenoceptor antagonist silodosin; it is used by elderly men to remove the symptoms of enlarged prostate such as urinary compression, frequency of urination, pauses when urinating, weak flow and incomplete bladder emptying(2,3).

MATERIALS AND METHODS:

In this study a sensitive, simple and accurate method was suggested for development of chromatographic method for the determination of solifenacin in pharmaceutical preparations. Analysis was carried out using an Agilent® HPLC unit equipped. The chromatographic separation was achieved using an Agilent Eclipse XDB C18 (150 × 4.6 mm, 5 µ) column, the mobile phase was made up of 10mM ammonium formate buffer (pH of 4), acetonitrile and methanol at a ratio of 55:32,5:12,5 v/v/v, running through the column at a flow rate of 1ml/min and with ultraviolet (UV) detection set at 210nm. Zolmitriptan is used as internal standart.

RESULTS:

Silodosin and the internal standard zolmitriptan eluted whose retention time were 1,52 and 2,45 minutes respectively. The method was validated for linearity in the working concentration range of 1-90µg/ml. Linearity was observed with a coefficient of determination (r2) of 0.9998. The recoveries obtained were all better than 101,2% and the limit of quantification and limit of detection were 0,9 µg/ml and 0.30 µg/ml, respectively.

CONCLUSIONS:

The proposed method was successfully used for the determination of solifenacin in pharmaceutical tablet with no significant interferences of excipients.

REFERENCES:

1. Kazuki K, Masaki Y, Yukio H (2006). British Journal of Urology International, 98: 1019–1024.
2. Deepak N et. al., (2014). Journal of Pharmaceutical and Biomedical Analysis, 88: 245-255.
3. Masaki Y, Imao M, Katsuyoshi A, Junzo K (2012). John Wiley& Amp; Sons, Somerset, NJ, 360–390.

P-271: DETERMINATION AND VALIDATION OF SOLIFENACIN IN PURE AND PHARMACEUTICAL DOSAGE FORMS VIA HPLC-UV

[1] Akman, CT., [2] Atila, A., [2] Senol, O., [2] Yaman, E., [2] Kadioglu, Y.

[1]Erzincan University, Faculty of Pharmacy, Department of Analytical Chemistry, Erzincan, Turkey

[2]Atatürk University, Faculty of Pharmacy, Department of Analytical Chemistry, Erzurum, Turkey

INTRODUCTION:

Overactive bladder (OAB) is a prevalent condition that has a significant impact on quality of life. The first-line pharmacological treatment commonly utilizes anticholinergic agents, which may be limited by their tolerability, efficacy, and long-term compliance. Solifenacine succinate, which is a chemical name [(3R)-1-azabicyclo [2.2.2] octan-3-yl] (1S)-1-phenyl-3,4-dihydro-1H-isoquinoline-2-carboxylate, butanedioic acid; is a selective M3 muscarinic antagonist and it is an anticholinergic and antispasmodic agent used in the treatment of urinary incontinence and overactive bladder syndrome (1). The aim of this study to develop simple, rapid, sensitive, reproducible and accurate method that can be applied to pharmaceutical preparations containing solifenazine.

MATERIALS AND METHODS:

In this study a sensitive, simple and accurate method was suggested for development of chromatographic method for the determination of the amount of solifenacin in pharmaceutical preparations. Analysis was carried out using an Agilent® HPLC unit equipped. The chromatographic separation was achieved using an Agilent Eclipse XDB C18 (150 × 4.6 mm, 5 µ) column, the mobile phase was made up of 10mM ammonium format buffer (pH of 4), acetonitrile and methanol at a ratio of 55:32,5:12,5 v/v/v, running through the column at a flow rate of 1ml/min and with ultraviolet (UV) detection set at a wavelength of 210nm. Zolmitriptan is used for internal standard.

RESULTS:

Solifenacin and the internal standard zolmitriptan eluted after 1,52 and 5,9 minutes respectively. The method was validated for linearity in the working concentration range of 1-60µg/ml. Linearity was observed with a coefficient of determination (r2) of 0,9998. The recoveries obtained were all above 99,7% and the limit of quantification and limit of detection were 1 µg/ml and 0.33 µg/ml, respectively.

CONCLUSIONS:

The proposed method was successfully used for the determination of solifenacin in pharmaceutical tablet with nosignificant interferences of excipients.

REFERENCES:

1. Finney SM, Andersson KE, Gillesple JI, Stewart LH (2006). BJU International, 98: 503-507.

P-272: DEVELOPMENT AND VALIDATION OF HPLC METHOD FOR SIMULTANEOUS DETERMINATION OF BETAMETHASONE DIPROPIONATE AND KETOCONAZOLE IN CREAM FORMULATIONS

[1] Karabulut, TC., [2] Amasya, G., [1] Kurbanoglu, S., [1] Ozkan SA.

[1]Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Topical corticosteroid betamethasone dipropionate (BET), which is a medium potency anti-inflammatory that is more potent than hydrocortisone and has anti-inflammatory, anti-pruritic and vasoconstrictive properties. Betamethasone in the cream formulations works by blocking the production of inflammatory chemicals, like prostaglandins and leukotrienes, which are hormone-like substances involved in the inflammatory process. It also narrows and constricts causes blood vessels that have become dilated (widened) and leaky allowing other inflammatory cells into the skin to escalate the inflammatory response. This reduces symptoms of inflammation associated with fungal infection. Ketoconazole (KET), a synthetic broad-spectrum antifungal is administered both in orally and topical formulations to treat a variety of fungal infections. This drug is classified as a BCS Class II due to its high permeability but low aqueous solubility.

MATERIALS AND METHODS:

There exists no literature for the simultaneous detection of BET and KET in fixed dose combination using liquid chromatography. Proposed study aimed to develop environmentally friendly, rapid, more sensitive and selective method for the simultaneous determination of BET and KET. This study also proposed a novel fixed dose topical formulation to enhance the solubility and permeability of active substances. The proposed HPLC method was applied to these formulations. On the other hand, validation

parameters such as accuracy, precision and recovery studies were also performed (1).

RESULTS:

In chromatographic separations, several mobile phase compositions and columns were tested for the efficient separation using system suitability parameters. Optimum chromatographic separation was achieved using a Thermo BDS Hypersil C18 (250 x 4.6 mm I.D.5 µm) column at a flow rate of 1.5 mL.min-1. The separation was carried out at 40 ºC and the UV detector adjusted to 239 nm.

CONCLUSIONS:

Finally, proposed methods were successfully applied for the simultaneous assay of the drug combination in pharmaceutical dosage forms with high recovery values for KET 99.85%, for BET 100.10%.

REFERENCES:

1. Gumustas M, Kurbanoglu S, Uslu B, Ozkan SA (2013). Chromatographia, 76(21-22):1365-1427.

P-273: FORMATION OF PT(II) - EPIRUBICIN METAL BASED COMPOUND IN ANALYTICAL CONDITIONS

[1] Adimcilar, V., [2] Cesme, M., [3] Unal, D., [1] Golcu, A.

[1]Istanbul Technical University, Faculty of Science and Letters, Department of Chemistry, Istanbul, Turkey

[2]Kahramanmaras Sutcu Imam University, Faculty of Art and Sciences, Department of Chemistry, Kahramanmaraş,Turkey

[3]Istanbul University, Faculty of Pharmacy, Department of Analytical Chemistry, Drug Research and Application Center, Istanbul, Turkey

INTRODUCTION:

Inorganic compunds have had gained great importance in the area of 'Medicinal Chemistry' which focuses on development of potential anticancer drugs. Preparation of various metal based anticancer drugs have been under study for several decedes and the milestone of these studies was the discover and the use of the cis-platinium ([Pt(NH3)2Cl2]) as an anticancer drug in 1969 (1). Although the cis-platinium is still the most frequently used chemotherapeutic drug today it has some drawbacks (2). Since then the researchers were focused on synthesis of novel and more convenient metal based drugs with using various metal ions such as Pt(II), Cu (II), Zn(II), Ru(III) and Mn(III). During the synthesis of the metal based complexes the drug molecules acts as ligands and generally donate their one or two pairs of electrons to the central metal atom. This work focussed on the design of a novel compound of Pt(II).

MATERIALS AND METHODS:

In the present study the Pt(II) based complex of the chemotherapeutic drug epirubicin (Fig) was synthesized in water-methanol mixture. The analytical conditions were investigated on the complex formation between central metal ion and epirubicin molecule such as time and pH. The T80 PG UV-Visible spectrometer, Agilent VNMRS 500 MHz NMR and LC-MS-MS instrument was used for characterization experiments.

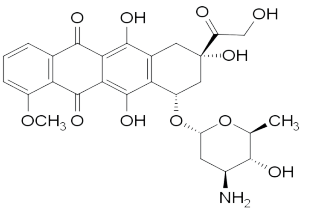


Fig: Epirubucin Structure

RESULTS:

The complex formation between drug that is the ligand molecule and metal ion was obtained by pH control. pH values greater than 7, the complex was obtained. Obtained Pt(II) based compound was characterized by using UV-visible spectroscopy and additionally by H-NMR and LC-MS-MS.

CONCLUSIONS:

A novel metal based compound was synthesized as a potential drug for treatment of cancer diagnossed patients where chemotherapeutic drugs were frequently in use.

Acknowledgements::This study was supported by a grant of Istanbul Technical University under TGA-2017-40917 project name.

REFERENCES:

1. Rosenberg B (1971). Plat. Met. Rev.,15: 42–51.
2. Dyson PJ, Sava G (2006). Dalton Transactions, 1929-1933.

P-274: ANALYSIS OF CORDYCEPIN AND ITS METABOLITES IN HELA CELLS BY LC-MS/MS

[1] Utami, W., [2] De Moor, C., [2] Barrett, DA.

[1]Universitas Muhammadiyah Surakarta, Faculty of Pharmacy, Surakarta, Indonesia

[2]University of Nottingham, School of Pharmacy, Nottingham, United Kingdom

INTRODUCTION:

Cordycepin (3'-deoxyadenosine) is a bioactive compound found in the caterpillar fungi (Cordyceps and Ophiocordyceps). These fungi are commonly used in traditional Chinese medicines and exhibits anti-inflammatory, anti-bacterial, antifungal, and anticancer effects (1-3). The accumulation of phosphorylated metabolites of cordycepin has been observed in some cell lines treated with cordycepin (4-5). However, the cellular metabolism of cordycepin still remains to be elucidated. Thus, the aims of this study are to develop a quantitative LC-MS/MS method for investigation the cellular metabolism of cordycepin and to observe the effects of cordycepin treatment on the cellular level of nucleotides in HeLa cells.

MATERIALS AND METHODS:

A LC-MS/MS method using the volatile ion pairing agent DMHA has been developed and established with the validation results. The method was used to analyse the metabolites of cordycepin in HeLa cells which treated with 50 µM cordycepin with or without 1 µM pentostatin for two, eight, and 24 hours .

RESULTS:

Cordycepin very rapidly converted to 3'-deoxyinosine in the cell culture medium and pentostatin could be inhibited this deamination. Cordycepin, cordycepin 5'-triphosphate, and 3'-deoxyinosine accumulated in cells with the triphosphate as its major metabolite. It also was observed that the drug treatment results in reduction of intracellular adenine nucleotides in HeLa cells.

CONCLUSIONS:

The LC-MS/MS method has been shown to have sufficient sensitivity and selectivity to measure the metabolites of cordycepin and the intracellular nucleotides. Using this method, the metabolism of cordycepin has been observed in HeLa cell and the cell culture medium as well. Cordycepin might contribute to induction intracellular of nucleotides depletion in HeLa cells at the long term, and this effect appeared to be enhanced by pentostatin.

ACKNOWLEDGEMENTS:

We gratefully acknowledge financial support from Islamic Development Bank.

REFERENCES:

1. Kim HG et al., (2006). European Journal of Pharmacology, 545(2-3):192-199.
2. Jeong JW et al., (2010). International Immunopharmacology, 10(12):1580-1586.
3. Paterson RRM (2008). Phytochemistry, 69(7):1469-1495.
4. Chen LS et al., (2008). British Journal of Haematology, 140(6): 682-691.
5. Kodama EN et al., (2000). Biochemical Pharmacology, 59(3): 273-281.

P-275: USE OF DAUBECHIES WAVELET FAMILY FOR THE ANALYSIS OF ATENOLOL AND CHLORTHALIDONE IN TABLETS

Ertekin, ZC., Dinc, E., Ardic, AH.

Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Atenolol (AT) is a selective beta-blocker and chlorthalidone (CH) is a diuretic agent. They have additive impacts on the cardiovascular system and are used for the treatment of hypertension (1). The tablets containing these two drug substances are commonly prescribed and efficient methods are needed for their analysis. The aim of the study was to develop a fast and reliable spectrophotometric method for the simultaneous analysis of AT and CH.

MATERIALS AND METHODS:

For the spectrophotometric determination of AT and CH, the overlapping spectral bands of these drugs were resolved by Daubechies 8-continuous wavelet transform (db8-CWT) method (2,3). The amplitudes at 244.1 nm and 224.9 nm were used for the determination of atenolol and chlorthalidone, respectively. Calibration equations were obtained by measuring the db8-CWT amplitudes in the concentration range of 6-30 µg/mL and 4-16 µg/mL for AT and CH, respectively. The proposed CWT method was validated by analyzing various binary synthetic mixtures of AT and CH.

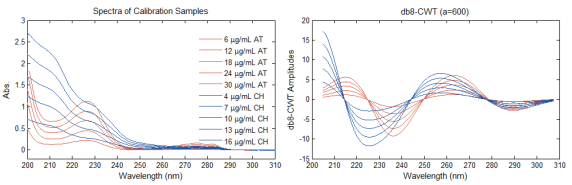


Figure 1. a) Zero-order absorption spectra of AT and CH b) db8-CWT absorption spectra of AT and CH

RESULTS:

After the validation studies, the proposed method was successfully performed to analyze the commercial samples. The assay results were found as 98.07 mg and 25.38 mg per tablet for AT and CH, respectively

(Label claim: 100 mg AT and 10 mg CH per one mL solution).

CONCLUSIONS:

The amounts of AT and CH in tablets were successfully determined by the use of Daubechies wavelet family without any separation step. This simple and accurate method is suitable for the routine analysis and quality control of the tablets containing AT and CH.

REFERENCES:

1. Seedat YK (1980). British Medical Journal, 281:1241-1243.
2. Dinc E, Baleanu D (2003). Jornal of Pharmaceutical and Biomedical Analysis, 31:969-978.
3. Ustundag et al., (2008). Revista de Chimie, 59:1387-1391.

P-276: MULTICOMPONENT ANALYSIS OF ROSUVASTATIN AND AMLODIPIN BY PARTIAL LEAST SQUARES AND PRINCIPLE COMPONENT REGRESSION

Ertekin, ZC., Dinc, E.

Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Spectrophotometry is the method of choice for a lot of laboratories owing to its simplicity and low-cost equipment. However, in case of overlapping spectra, classical spectrophotometric methods fail to perform analysis of mixtures. Partial least squares (PLS) and principle component regression (PCR) methods are standard techniques devoted to multicomponent analysis of mixtures (1,2). The aim of this study was to develop simple and reliable spectrophotometric methods for to quantify rosuvastatin (ROS) and amlodipine (AML) in tablets without a separation step.

MATERIALS AND METHODS:

Standard solutions containing ROS and AML were prepared between 2-48 µg/mL for both drugs. After recording their absorbance spectra between 200-400 nm, PLS and PCR calibrations were obtained using the nominal concentrations (y-block) and absorbance data (x-block). Number of factors were determined by cross-validation method. The regression coefficients of PLS model were reported to be 0.9994 and 0.9998 for ROS and AML, respectively. In case of PCR model, the values of regression coefficients for ROS and AML were calculated as 0.9991 and 0.9995, respectively. For the validation of the methods, synthetic mixtures, standard addition, intra- and inter-day samples were analyzed. Then, the sample analysis was performed using these methods without any separation step.

RESULTS:

The recovery percentage values obtained by PLS were 101.8 for ROS and 89.7 for AML, whereas by PCR model, the recovery percentage values were reported to be 99.4 and 103.1 for ROS and AML, respectively. Tablet analysis results were summarized in Table 1.

Table 1. Tablet analysis results. (Label claim: 20 mg ROS/10 mg AML per tablet)

	PLS (mg/tablet)		PCR (mg/tablet)	
	ROS	AML	ROS	AML
Mean*	20.6	10.2	20.4	9.99
Standard deviation	0.19	0.12	0.18	0.12
Relative standard deviation	0.90	1.18	0.89	1.22

** n = 10*

CONCLUSIONS:

The proposed multivariate methods were found to be simple, fast and suitable for the analysis of ROS and AML in tablets. These methods did not require any separation method for the multicomponent analysis.

REFERENCES:

1. Nevado et al., (1997). Analytica Chimica Acta, 340:257-265.
2. Dinc et al., (2008). Journal of Pharmaceutical and Biomedical Analysis, 48:1471-1475.

P-278: SOLIDIFICATION OF FLOATING ORGANIC DROP MICROEXTRACTION OF PIPERINE FROM BLACK AND WHITE PEPPER PRIOR TO ITS DETERMINATION BY HPLC

Ur Rahman, Z., Caleb, J., Al Nidawi, M., Alshana, U.

Near East University, Faculty of Pharmacy, Department of Analytical Chemistry, Nicosia, TRNC

INTRODUCTION:

Solidification of floating organic drop microextraction (SFODME) has recently been developed by Leong and Huang (1) in which a mixture of an organic extraction solvent with lower density than water, low toxicity and melting point near room temperature (in the range of 10–30 °C) and a disperser solvent such as methanol, ethanol and acetonitrile are used. In this study, SFODME was used prior to high-performance liquid chromatography (HPLC) for the extraction of piperine from black and white pepper from different origins.

MATERIALS AND METHODS:

A 1200 SERIES Agilent Technologies Gradient HPLC equipped with a Diode-Array Detector (DAD), and a reversed-phase column (i.e., Agilent Eclipse XDB-C18. 4.6 mm ID 150 mm, 5 µm) was used for separating the analyte from other matrix components using a mobile phase composition of 45/55 (%, v/v) ACN/H2O, 5 µL injection volume, at ambient temperature and a flow rate of 1.2 mL min-1. Piperine was monitored at its maximum absorption wavelength of 346 nm using DAD. All chemicals used in this study were at least of analytical reagent grade.

RESULTS:

Piperine was extracted from the solid sample (0.10 mg) into ACN by salting-out extraction, which was then used as the disperser solvent in SFODME. Optimum extraction conditions were as follows: 50 µL of 1-dodecanol (extraction solvent), 950 mL of acetonitrile (disperser solvent) and 60 s extraction time. The analyte was back-extracted into 150 µL of 50 mM acetic acid in 45/55 (%, v/v) ACN/H2O before being injected into HPLC. Calibration graphs showed good linearity with coefficients of determination () higher than 0.9964. Relative standard deviations (%RSD) for intra- and interday precisions were lower than 5.2 and 11.3, respectively. Limits of detection (LOD) ranged from 7.5 to 10.8 mg g-1 with a recovery of 95.0% or higher.

CONCLUSIONS:

The proposed method was proven to be fast, cost-effective and relatively green compared to the use of heavy chlorinated solvents for the extraction of piperine from white and black pepper.

ACKNOWLEDGEMENTS:

This study was supported by a BAP Project of Near East University (SAG-2016-2-022)

REFERENCES:

1. Leong MI, Huang SD (2008). Journal of Chromatography A, 1211:8-12.

P-279: DEVELOPMENT AND VALIDATION OF A SELECTIVE HPLC METHOD FOR THE DETERMINATION OF S-ADENOSYL L-METHIONINE ISOMERS FROM RAT PLASMA

[1] Ergin, AD., [2] Gumustas, M., [3] Ozcelikay, T., [1] Yuksel, N., [4] Ozkan, SA.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

[2]Ankara University, Institute of Forensic Sciences, Department of Forensic Toxicology, Ankara,Turkey

[3]Ankara University, Faculty of Pharmacy, Department of Pharmacology, Ankara, Turkey

4Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

S-adenosyl-L-methionine (SAMe) is an endogenic methyl donor naturally present in all cells. It is involved in many chemical reactions primarily in methylation. SAMe is an important alternative in the treatment of depression due to its non-toxic and endogenic nature (1).

SAMe has two diastereoisomers. While S,S diastereoisomer is active, R,S diastereoisomer is inactive. However, there is not enough method for the separation of these two diastereoisomers (2).

The aim of the present work is to develop and validate a selective High Performance Liquid Chromatography (HPLC) method for the selective and sensitive determination of S- Adenosyl L Methionine (SAMe) from its bulk form and rat plasma samples.

MATERIALS AND METHODS:

Shimadzu Prominence-LC2030C HPLC system with UV detector was used for method development and validation studies.

A Kinetex F5 (150x4,6 mm, 5 µm; Phenomenex, USA) analytical column was selected as stationary phase due to its separation ability for the diastereomers. An isocratic mobile phase consisting of 0.45 % Trifluoroacetic acid, 5 mM ammonium acetate buffer (pH 4.0) was used in whole study. In order to optimize the chromatographic conditions, effects of injection volume, column oven temperature and flow rate were also examined. Finally, optimized method was validated in accordance to the International Council on Harmonization (ICH) guidelines by the means of precision, linearity, accuracy, etc.

RESULTS:

Optimized conditions can be summarized as follows; 20 µL injection volume; 0.8 mL.min-1 flow rate and 25°C column oven temperature. The retention times for both isomers were obtained less 10 min. Developed method was found linear in the range between 25 and 4000 ng.mL-1 with correlation coefficient of 0.9995. Accuracy and applicability of the method was demonstrated by the application of rat plasma samples after extraction steps.

CONCLUSIONS:

A sensitive and selective HPLC method was developed for the determination of diastereomers of SAMe from bulk form and rat plasma samples with high recovery values.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAGS115S339)

REFERENCES:

1. Bottiglieri T (2002). Am J Clin Nutr., 76
2. Zhang J, Klinman JP (2015). Analytical Biochemistry 476: 81–83

P-280: IN VITRO EVALUATION OF CAPSAICIN PATCHES FOR TRANSDERMAL DRUG DELIVERY

[1] Uzunovic, A., [2] Osmancevic, S., [1] Pilipovic, S., [3] Sapcanin, A., [2] Ademovic, Z.

[1]Agency for Medicinal Products and Medical Devices, Sarajevo, Bosnia and Herzegovina,

[2]University of Tuzla, Faculty of Pharmacy, Tuzla, Bosnia and Herzegovina,

[3]University of Sarajevo, Faculty of Pharmacy, Sarajevo, Bosnia and Herzegovina.

INTRODUCTION:

Capsaicin has been employed topically to treat some peripheral painful states, such as rheumatoid arthritis, cancer pain and diabetic neuropathy. The high degree of pre-systemic metabolism of intragastric capsaicin and very rapid elimination half-life of capsaicin made topical application of capsaicin advantageous. The aim of this study was to evaluate differences in the dissolution characteristics of capsaicin patches purchased from the local market (formulation I, II and III).

MATERIAL AND METHODS:

The fabricated patch area contains 18-145 µg of capsaicin/cm2 of adhesive. USP Apparatus 5 (Paddle Over Disc) is used for transdermal patch testing at fixed rotation speed (50 rpm). The fabricated patch was cut into 9 cm2 and placed against a disc (delivery side up) retained with the stainless-steel screen and exposed to 500 mL of phosphate buffer solution pH 4.0. All dissolution studies were carried out at 32± 0.5°C and samples were collected at various time intervals (60 and 240 minutes) and analyzed for capsaicin content using high-performance liquid chromatography (HPLC). Optimized and Validated HPLC method uses a ProntoSIL 120-3-C18AQ 125x4.0 mm (3µm) column maintained at 600C. The mobile phase consisted of acetonitrile: water (50:50v/v), the flow rate of 0.9 mL/min, the injection volume 10µL and the detection wavelength 222nm (1).

RESULTS:

According to the results obtained in this study, we can conclude that the relative difference of dissolution rate of capsaicin was slightly decreased after 240 minutes: formulation I vs II (2.9± 0.3%), formulation I vs III (3.3± 0.2%) and formulation II vs III (0.29± 0.07%).

CONCLUSIONS:

Although several apparatus and procedures (USP apparatus 5, 6, 7 and a paddle over extraction cell method) have been used to study in vitro release characteristics of transdermal patches, USP Apparatus 5 could be considered as a discriminatory test that would be able to point out the differences in the dissolution rate of all tested capsaicin patches at short sampling intervals (60 and 240 minutes).

REFERENCES:

1. Al Othman ZA, Ahmed YBH, Habila MA, Ghafar AA (2011). Molecules, 16:8919-8929.

P-281: IN VITRO STUDIES OF THE ORALLY DISINTEGRATING TABLET FORMULATIONS CONTAINING MIRTAZAPIN

Arslan A., Atalay F., Esim O., Köse Ozkan C., Tas C., Savaser A., Ozkan Y.

University of Health Science, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Mirtazapine is an active ingredient used in antidepressant drugs in tetracyclic form. Besides an antidepressant effect, it also shows an anxiolytic character (1). Mirtazapine has slightly hygroscopic properties, however it is insoluble in water, freely soluble in methanol (2). Mirtazapine has many orally disintegrating tablet formulations in the market. The aim of this study was to develop a new dissolution method for orally disintegration tablets.

MATERIALS AND METHODS:

The mirtazapine used in the study is a kindly gift by Abdi İbrahim company (Istanbul, Turkey). UV spectrophotometer was used for quantitative analysis of mirtazapine. The calibration graph and standard linear equation of mirtazapine solutions with different concentrations prepared by serial dilution was obtained using the method of Özdemir et al. (3). Disintegration tests of mirtazapine-containing tablets were performed. Artificial saliva fluids with and without carbopol were prepared and permeability studies of tablets were carried out on the Franz diffusion cell during the period of dispersion. After that, the dissolution rate profiles of donor compartment contents were evaluated by simulating the gastrointestinal medium, using USP Apparatus II.

RESULTS:

The spectrophotometric method applied for quantitative analysis provides a fast and effective solution. Disintegration test results of tablets were meet the compendial requirements. Permeability differences and dissolution profiles, which they exhibited in two different artificial saliva fluid mediums, were evaluated. It has been found that the pass through the membrane is very limited.

CONCLUSIONS:

It has been found that the membrane permeation of the mirtazapine-containing tablet formulations of the appropriate physicochemical properties is negligible, so that liquid chromatographic methods may be preferred for quantitative analysis, on the other hand USP Apparatus II is considered to be sufficient for dissolution studies.

REFERENCES:

1. Sitsen JMA.,Moors J (1994). Drug Investigation, 8(6), 339-344.
2. Sweetman CS (2009). Martindale, The Complete Drug Reference, Thirty-sixth edition. United Kingdom and United States of America, pp 409-411.
3. zdemir EK, Ulu ST, Ozdemir D, Ozgur EK, Ulu ST, Unal DO (2012). Journal of Faculty Pharmacy of Istanbul University, 2(42 (2)), 77-82.

P-282: EXTENDED RELEASE PLGA NANOPARTICLES FOR CHRONIC PAIN

[1] Ozturk AA., [2] Banderas LM, [2] Cayero Otero M, [1] Yenilmez E., [1] Yazan Y.

[1] Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Eskişehir, Turkey

[2] University of Seville, Faculty of Pharmacy, Department of Pharmacy and Pharmaceutical Technology, Seville, Spain

INTRODUCTION:

The pain situation has a very important effect on the biological, psychological, sociological and economic situation of the patient (1). Dexketoprofen trometamol (DT) has been developed as a water-soluble trometamine salt. DT is a rapidly acting analgesic agent in the treatment of painful musculoskeletal disorders such as back pain and osteoarthritis (2). In this study; DT loaded PLGA Nanoparticles (NPs) formulated with Double emulsions Solvent evaporation method which is the most suitable method for preparing PLGA NPs for hydrophilic drugs.

MATERIALS AND METHODS:

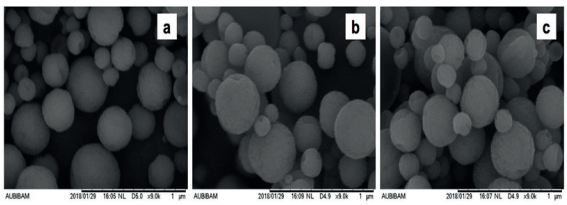
PLGA-based NPs were prepared by following the 'Double Emulsification Solvent Evaporation Technique'. Structures of nanoparticles were characterized by particle size (PS) and zeta potential (ZP) measurements, morphology, thermal analysis (DSC), X-ray difraction (XRD) , FTIR and 1H-NMR.

RESULTS:

Table 1. Result of particle size, PDI, zeta potantial

Code	PS(nm)±SD	PDI±SD	ZP(mV)±SD	EE%±SD
Alp-blank	295.7 ± 2.9	0.101 ± 0.015	-29.59 ± 0.23	-
Alp-5	243.8 ± 5.3	0.062 ± 0.024	-27.26 ± 0.92	64.194 ± 0.484
Alp-10	251.9 ± 2.8	0.075 ± 0.020	-26.48 ± 0.63	49.239 ± 1.129

Figure 1. SEM images of PLGA NPs a: Alp-blank b: Alp-5 c: Alp-10



CONCLUSIONS:

NPs were prepared for chronic pain by Double Emulsification Solvent Evaporation Technique'. The PS, PDI, ZP, DSC, XRD, FT-IR and 1H-NMR analysis of formulations justified that DT was incorporated into PLGA NPs successfully.

ACKNOWLEDGEMENTS:

This study was financed by Anadolu University Scientific Research Project Foundation (No: 1708S471). We also thank University of Seville, Faculty of Pharmacy, Department of Pharmacy and Pharmaceutical Technology for giving us all their opportunities.

REFERENCES:

1. Mainardi F et al.(2014) Dexketoprofen Trometamol in the Acute Treatment of Migraine Attack: A Phase II, Randomized, Double-Blind, Crossover, Placebo-Controlled, Dose Optimization Study. J Pain 15(4):388-394.
2. Öztürk AA et al.(2017) Dexketoprofen Trometamol-Loaded Kollidon® SR and Eudragit® RS 100 Polymeric Nanoparticles: Formulation and In Vitro-In Vivo Evaluation. Lat Am J Pharm 36(11):2153-2165.

P-283: CARVEDILOL LOADED PLGA NANOPARTICLES FOR HYPERTENSIVE TREATMENT

[1] Ozturk AA., [2] Martin BL., [2] Cayero Otero, MD., [1] Yenilmez E., [1] Yazan Y.

[1] Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Eskişehir, Turkey

[2] University of Seville, Faculty of Pharmacy, Department of Pharmacy and Pharmaceutical Technology, Seville, Spain

INTRODUCTION:

Hypertension (HT), which defines systolic blood pressure as >140 mmHg or diastolic blood pressure >90 mmHg. There are now several drugs that are available in the market, including carvedilol (CVL) which is used for the management of cardiovascular disease and HT (1). CVL-containing PLGA nanoparticles (NPs) were prepared by nanoprecipitation method.

MATERIALS AND METHODS:

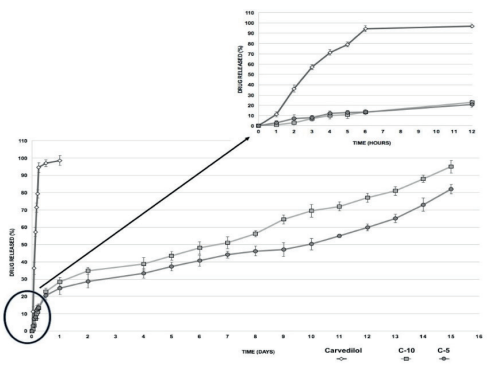
PLGA-based NPs were prepared by following the nanoprecipitation technique with modification (2). Structures of nanoparticles were characterized by particle size (PS) and zeta potential (ZP) measurements, morphology, thermal analysis (DSC) and FTIR. The entrapment efficiency (EE%) and dissolution study of each formulation was performed with HPLC. In vitro release study of the NPs formulations was investigated over 10 days and that performed in phosphate buffer (pH 6.8) containing 30 % PEG 400. Data obtained from the in vitro drug release studies were further investigated for release kinetics using DDSolver software program.

RESULTS:

Table 1. Result of PS, PDI, ZP and EE% (n=3)

Code	PS (d.nm), mean±SD	PDI, mean±SD	ZP (mV), mean±SD	EE %, mean±SD
C-Blank	173.2±1.5	0.175±0.014	-24.9±2.5	-
C-5	326.3±8.3	0.164±0.035	-25.9±0.9	79.356±4.605
C-10	345.0±3.8	0.128±0.071	-26.6±1.8	68.765±3.519

Figure 1. In vitro dissolution profile of prepared formulation and pure CVL



CONCLUSIONS:

The PS, PDI, ZP, DSC, FT-IR analysis of formulations justified that CVL was incorporated into PLGA NPs successfully. NPs formulations is promising to be for extended delivery of CVL with succesfully loaded and Peppas-Sahlin kinetic model was found to fit best to carvedilol release from nanoparticles.

ACKNOWLEDGEMENTS:

The authors would like to thank University of Sevilla, Faculty of Pharmacy, Department of Pharmacy and Pharmaceutical Technology is appreciated for offering their study facilities.

REFERENCES:

1. Kipriye Z et al. (2017) Preparation and evaluation of carvedilol-loaded solid lipid nanoparticles for targeted drug delivery. Trop J Pharm Res, 16(9): 2057-2068.
2. Martín Banderas L, et al. (2012) Cannabinoid derivate-loaded PLGA nanocarriers for oral administration: formulation, characterization, and cytotoxicity studies. International Journal of Nanomedicine 7:5793-5806

P-284: DETERMINING THERAPEUTIC RESPONSE OF MULTIPLE MYELOMA BY MASS ACCUMULATION AT SINGLE CELL LEVEL

[1,2] Cetin, AE., [2,3] Stevens, MM., [2] Calistri, NL.,[3] Fulciniti, M., [2] Olcum, S., [2] Kimmerling, RJ., [3] Munshi, N., [2] Manalis, SR.

[1]Izmir Dokuz Eylul University, International Biomedicine and Genome Institute, Izmir, Turkey

[2]Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology, Cambridge, MA, USA

[3]Harvard Medical School, Dana-Farber Cancer Institute, Boston, MA, USA

INTRODUCTION:

Multiple myeloma (MM) is the second most common hematologic malignancy in the world. Despite improvement in outcome, the disease is still incurable for most patients. With the same treatment, patient survival varies, suggesting that there is an underlying heterogeneity in the disease. Therefore, a clear delineation of heterogeneity in therapeutic response could provide unique opportunities for personalized treatment of myeloma.

MATERIALS AND METHODS:

Here, we introduce an approach for defining the sensitivity of single cells using an apparatus called suspended microchannel resonator (SMR) (1). By measuring the mass repeatedly in a device configuration with multiple SMRs connected in serial, where each SMR is separated in time by delay

channels, we can determine cell growth (Figure A). Mass accumulation rate (MAR) is a measurement of the rate at which the cells gain mass (Figure B). The platform can measure ~100 cells per hour and over a 20-minute period, each cell is weighed 10 times, which is enough to get an accurate MAR measurement (Figure C). A decrease in MAR following drug treatment means the cells are sensitive to the drug, but if they are resistant, there is no change in MAR.

RESULTS:

We tested a variety of drugs on tumor cells from MM patients. For each patient, we tracked the cells' response to different drug combinations including bortezomib, dexamethasone, and lenalidomidev (Figure C). We showed an excellent correlation between our MAR tests and the outcomes seen in patients, as measured by clinical protein biomarkers found in the bloodstream, which are classically used by doctors to determine whether a drug is killing the tumor cells (1).

CONCLUSIONS:

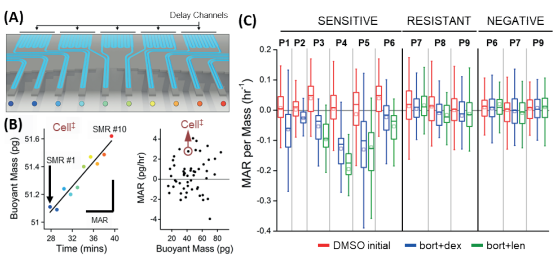
The major outcome of this work is to open doors for personalized medicine. At the point of a bone marrow biopsy, we would be able to inform the clinicians as to which therapy or combinations of therapies the patient seems to be most sensitive.

Acknowledgements:

We acknowledge Bridge Project, a partnership between Koch Institute for Integrative Cancer Research and Dana-Farber Cancer Institute.

References

1. Cetin et al., (2017). Nature Communications, 8:1613.



P-285: EVALUATION OF PHYSICOCHEMICAL CHARACTERIZATION OF BERBERINE FOSPHOLIPID COMPLEX

[1] Karatas, A., [2] Gungor, A.,

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

[2]Bulent Ecevit University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Zonguldak, Turkey

INTRODUCTION:

Transfer of plant-derived active ingredients to the modern treatment is becoming increasingly common. However, a significant portion of these active ingredients have long side chains and high polarities. This acts as a barrier to absorption by passive diffusion through the gastrointestinal mucosa or skin. At this point, the new complexing technique denominated "phyto- phospholipid complex" or "phytosomes" plays an important role in easing absorption and increasing bioavailability (1). Berberine (BER) has been demonstrated to posses various pharmacological functions. However, due to its poor aqueous solubility and low gastrointestinal absorption. The phospholipid-drug molecular complexation technique has improved the lipophilicity of drug, reduced adverse drug effects and enhanced bioavailability and therapeutic efficacy of drug. The primary goal in this project is preparing the BER-phospholipid complex which was reported to have low absorption and bioavailability The physicochemical properties of the complex obtained by optimal parameters were investigated by means of differential scanning calorimetry (DSC), Fourier transform infrared (FTIR) and N-octanol/water partition coefficient (Po/w).

MATERIALS AND METHODS:

Thermograms of BER, phospholipid, BER-phospholipid physical mixture and BER complex were recorded to study the thermal behavior by a DSC. FTIR analysis of the BER-phospholipid complex was used to investigate the interaction between BER and phospholipid. The BER, phospholipid and physical mixture and BER-phospholipid complex were used as controls for comparison. The Po/w of BER-phospholipid complex were determined by the usual agitation method.

RESULTS:

It has been shown that berberine-phospholipid complex could be successfully prepared. The crystallographic and thermal analysis results has indicated that the BER complexed with phospholipid was in an amorphous form. The Po/w of BER-phospholipid complex studies showed BER phospholipid complex increased the lipophilicify of BER.

CONCLUSIONS:

Our studies demonstrated that may have the potential for facilitating the oral drug delivery of BER.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-215S664).

REFERENCES:

1. Khan J et al., (2013). Journal of Controlled Release, 168(1):50-60.

P-286: DEVELOPMENT SOFT GELATIN CAPSULE CONTAINING IBUPROFEN.

[1] Mehmetoglu, A., [1,2] Karasulu, E., [1,2] Yildiz Turkyilmaz, G.

[1]Ege University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Biopharmaceutical and Pharmacokinetics Izmir, Turkey

[2]Ege University, Center for Drug Research & Development and Pharmacokinetic Application, ARGEFAR, Izmir, Turkey

INTRODUCTION:

Ibuprofen, a propionic acid derivative, is a nonsteroidal anti-inflammatory drug used for the treatment of pain and inflammation. Ibuprofen is a poor water soluble drug (1). So that in this study we have aimed to investigate the solubility of ibuprofen in different oils, surfactants, co-surfactants and buffers and develop a soft gelatin capsule formulation containing 200 mg Ibuprofen.

MATERIALS AND METHODS:

Solubility studies of ibuprofen were carried out by shaking an excess amount of each drug with 1 mL of the different oils (oleic acid etc.), surfactants(Tween 80 etc), co-surfactants(Transcutol HP etc.) and buffers(3). The samples were incubated in a 37 ℃ water bath at 150 rpm for 48 hours. After 48 hours, the samples were centrifuged in Sigma centrifuge at 3000 rpm for 15 minute. The supernatants were collected and injected into HPLC (Schimadzu HPLC-PDA) vials for analysis. After, a high-performance liquid chromatography (HPLC) method was developed and validated for determination of ibuprofen and 4 impurities (impurity A, impurity F, impurity J and impurity N). The method, a gradient condition of mobile phase A containing 0.1 M Disodium hydrogen phosphate buffer (pH 6.9) and mobile phase B containing acetonitrile, at a flow rate of 1.0 mL/ minute with C18 (INERSTIL (ODS 3), 150×4.6 mm,5µm,Hichrom) column, 224nm as wavelength (2), was validated according to ICH guideline. The method showed excellent linear response with correlation coefficient (R2) values of 0.999. We have developed different soft gelatin capsule formulations with the combination of appropriate compounds mentioned above and performed the dissolution studies with USP Apparatus 1 (37ºC, 150 rpm, 900 mL phosphate buffer pH 7.2) to compare the test formulations with the reference formulation(Advil Liquid Gels 200mg).

RESULTS:

As a result of the solubility studies we have chosen some combinations of appropriate compounds mentioned above. According to our dissolutions results we have calculated f1-f2 value by comparing the test formulations with reference product.

CONCLUSIONS:

We have chosen the formulation with the highest similarity as our final test formulation according to f1-f2 value obtained by comparing the developed formulations with reference product.

ACKNOWLEDGEMENTS:

This project is granted by Ege University, Committee of Scientific Research Project (BAP).

REFERENCES:

1. Bharat Bhushan S, Surjyanarayan M (2013). Journal of Pharmaceutics, 6 pages.
2. Henry F, Lynda L, Michael G (2002). Chromatographia, 1353-1360.
3. Liandong H, Jianxue Y, Wei L (2011). Drug Delivery, 90-95.

P-287: ENCAPSULATION OF ELETRIPTAN HYDROBROMIDE IN PLGA NANOPARTICLES BY W/O/W EMULSIFICATION SOLVENT EVAPORATION METHOD

Savaser, A., Esim, Ozgur., Ozkan, CK., Tas, C., Ozkan, Y.

University of Health Sciences, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Eletriptan Hydrobromide is a second generation triptan class drug designated as R-3-[(1-methyl-2-pyrrolidinyl) methyl]-5-[2-(phenyl sulfonyl) ethyl]-1hindole mono hydrobromide with a molecular weight of 463.40 g/mol. It is used to treat migraine but not prevention (1). The objective of this study was to develop a modified W/O/W double emulsion process using dichloromethane as organic solvent to prepare Eletriptan Hydrobromide loaded nanoparticle with high yield, high entrapment efficiency.

MATERIALS AND METHODS:

PLGA nanoparticles were prepared using the W/O/W emulsion technique. Briefly, different amount of Eletriptan Hydrobromide and PVA was dissolved into 1 ml of distilled water (internal aqueous phase) and then added to 3 ml of dichloromethane containing PLGA (oil phase). The primary W /O emulsion was

prepared by a probe sonicator (Bandelin, Germany) at 30 W for 45 s. The primary emulsion was re-emulsified with the external aqueous phase containing PVA and 10 mL distilled water (external aqueous phase), using the probe sonicator at 50 W for 60 s. Afterwards, the organic solvent was evaporated using rotary evaporator.

RESULTS:

The difference in the particle sizes, zeta potentials, PDI and EE% of the nanoparticles prepared with W/O/W emulsification method that the water pH plays a key role on the resultant nanoparticle encapsulation efficieny

CONCLUSIONS:

It can be concluded from the study that it is possible to prepare Eletriptan Hydrobromide −PLGA nanoparticles using double emulsification solvent evaporation method. The effects of variations in the drug, polymer, surfactant concentrations were evaluated through changes in the size of the nanoparticles. F4 was predicted as the optimal formulation with minimum polydispersity index. However encapsulation efficiency was found 43,24±5,19 % and this result can be enhanced by changing polymers, surfactants or preparation methods. As further studies, this nanoparticles can be used in various root of administration for drug delivery studies.

ACKNOWLEDGEMENTS:

This study was supported by a grant of University of Health Sciences (BAP-2017/006)

REFERENCES:

1. Esim O, et al. Journal of Pharmaceutical and Biomedical Analysis 142 (2017): 74-83.

P-288: THE EFFECT OF POLYMERIC STABILIZER ON STABILITY OF OPTIMUM FLURBIPROFEN NANOSUSPENSION

Oktay, A., Karakucuk, A., Ilbasmis Tamer, S., Celebi, N.

Gazi University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Flurbiprofen (FB) is one of non-steroidal anti-inflammatory drugs. Its low water solubility causes lower bioavailability. To solve this problem FB nanosuspensions are prepared. However, nanosized particles demonstrate tendency toward agglomeration or crystal growth; so, they should be stabilized with stabilizers (1). The aim of this study is to evaluate the physical stability of optimum FB nanosuspension with stabilized polymeric stabilizer during 6 months.

MATERIALS AND METHODS:

24 (2 levels, 4 factors) full factorial design using Design Expert® Software Version 9 was employed to optimize of the FB nanosuspension. The four independent variables and two levels studied in this investigation were, percentage of FB (1%- 4%) FB: stabilizer ratio (1:4, 4:1), type of stabilizer (HPMC-PVP), homogenization cycle (10 pass-30 pass). FB nanosuspensions were prepared using Microfluidics LV1 (Microfluidizer® USA). To characterize the formulation and investigate the physical stability of optimum formulation particle size (PS), polydispersity index (PDI) and zeta potential (ZP) values were measured during 6 months (initial, 1., 7.,15. days, 1.,3.,6. months) at 25°C. The results were evaluated using univariate ANOVA at $p<0.05$ as the minimum level of significance.

RESULTS:

DoE results showed that PS values decreased at high level of FB:stabilizer ratio regardless of type of stabilizer. When PVP is used as a polymeric stabilizer, the percentage of FB should be higher to obtain lower PDI. High percentage of FB also provides to obtain higher ZP values. According to these results; optimum formulation was determined with these parameters: PVP as a stabilizer; 4% as percentage of FB and 4:1 as FB:PVP ratio and 10 cycle as a homogenization cycle. HPMC stabilized nanosuspension was obtained with these optimum parameters and its stability compared with PVP stabilized nanosuspension. Up to one month, PS increased from 837,70±14,64 nm to 1060±10 nm for PVP stabilized nanosuspensions and from 1151,67±36,75 to 1686,67±6,35 nm for HPMC stabilized nanosuspensions at 25°C. The PDI values did not change significantly during six months ($p>0.05$). On the basis of ZP; whereas it was found lower than initial value after one week, by the end of six months ZP values were found constant.

CONCLUSIONS:

Optimum formulation stabilized with PVP was found better to improve stabilization of FB nanosuspensions comparison with HPMC at 25°C during six months.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (117S149)

REFERENCE:

1. Verma S, Kumar S, Gokhale R, Burgess DJ (2011). International Journal of Pharmaceutics, 406:145–152.

P-289: INVESTIGATION OF HEALTH MINISTRY OF LICENSED BIOTECHNOLOGICALLY MEDICINES FOUND IN PHARMACIES IN TURKEY

Onbasli, D., Yuvali Celik, G., Ceylan, A., Dal, A.

Erciyes University, Department of Pharmaceutical Biotechnology, Kayseri, Turkey

INTRODUCTION:

The importance of biotechnology in the healthcare field and the pharmaceutical industry is increasing day by day. So, recently, the use of biotechnological drugs has begun to come into being from traditional medicines (1). In the health field, new biotechnological drugs have begun to be produced with the development of technologies like Recombinant DNA Technology, Monoclonal Antibody Technology. In this study, found in pharmacies in Turkey in 2017, the ministry of health licensed biotechnological active ingredients of drugs, mechanism of action, approved indications, the preparations containing these active ingredients in these drugs and the pregnancy category of these drugs by considering it is aimed to understand the number of these drugs, the place of treatment and the importance of the treatment.

MATERIALS AND METHODS:

RxMediaPharma® 2017, on the basis of domestic and imported biotechnological drugs in Turkey were scanned..

RESULTS:

In this study, a total of 191 active substances, either in the research phase or in the preparation phase, were identified, 5 of which were imported from domestic sources, 212 imported from drugs including these active substances and only 83 of them were biotech drugs licensed by the Ministry of Health.

CONCLUSIONS:

Located in pharmacies in Turkey in 2017, the Ministry of Health licensed 83 units biotechnological drugs have been identified.

ACKNOWLEDGEMENTS:

The authors would also like to thank to Muberra Kurt for her help.

REFERENCES

1. Gül UD (2014). Bilecik Şeyh Edebali Üniversitesi Fen Bilimleri Dergisi, 1(1): 67-68

P-291: DESIGN AND EVALUATION OF ORODISPERSIBLE TABLETS (ODTS) CONTAINING CARBAMAZEPINE AND LEVETIRACETAM

Kandilli, B., Ugur, AB., Cetin, M.

Ataturk University, Department of Pharmaceutical Technology, Erzurum, Turkey

INTRODUCTION:

Levetiracetam (LEV) and carbamazepine (CBZ) are antiepileptics and synergistic effect is observed when used together (1). Oral disintegrating tablets (ODTs) have advantages for patients with swallowing difficulty and improve patient complience, especially geriatric and pediatric groups (2). The aim of this study is to formulate LEV+CBZ ODTs by lyophilization method.

MATERIALS AND METHODS:

LEV and CBZ were generous gifts from DEVA Holding A.Ş. (İstanbul, Türkiye) and Biofarma İlaç San. Tic. A.Ş. (İstanbul, Türkiye), respectively. LEV+CBZ ODTs were prepared by lyophlization method and quality control tests (thickness, diameter, hardness, friability, weight variation, in vitro dispersion time and dissolution). In vitro dispersion time was measured by dropping ODT in a glass cylinder containing 6 mL pH 6.8 of simulated saliva fluid or water (for each, n=6). The in vitro dissolution study was performed in pH 6.8 phosphate buffer containing %5 Tween 80 using USP apparatus II (at 50 rpm) and at 37ºC.

RESULTS:

The mean diameter and thickness of ODTs (n=20) were 16.870±0.113 mm and 5.120±0.111 mm, respectively. The average hardness of ODTs was 11.960±2.204 N and also, the percentage friability for ODTs was within the limit (<1%). Weight variation was found as 0.363±0.005 g and none of ODTs were found to deviate from average weight of tablets. In addition, in vitro dispersion time was less 30 sec (7.917±1.569 sec in water and 15.675±1.822 sec in SSF). 99.481±2.755% (LEV) and 99.899±3.822% (CBZ) of drugs were dissolved in dissolution medium within 10 and 30 minutes at 37±2 ºC, respectively (Figure 1).

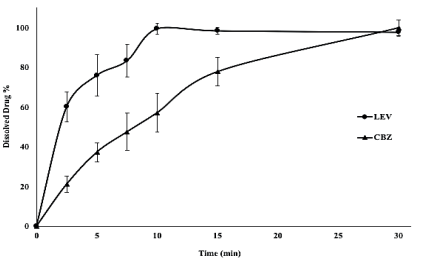


Figure 1. Dissolution profiles of ODTs (n=6).

CONCLUSIONS:

Lyophilized LEV+CBZ ODTs were successfully prepared and they might be useful for treatment of epilepsy.

REFERENCES:

1. Kaminski et al (2009). Epilepsia, 50(3): 387-397.
2. Abay FB, Ugurlu T (2015). J Pharm Drug Devel 3(3):303.

P-292: INVESTIGATION OF THE SOLUBILITY OF NYSTATIN AND NIFURATEL FOR SELECTING THE APPROPRATE DISSOLUTION MEDIA FOR THE OVULE FORMULATION

[1] Ayan, C., [1,2] Karasulu, E.

[1]Ege University, Center for Drug Research & Development and Pharmacokinetic Application, ARGEFAR, Izmir, Turkey

[2]Ege University, Faculty of Pharmacy, Pharmaceutic Technology Department, Izmir, Turkey

INTRODUCTION:

Intravaginal administration is an alternative drug administration route because of vagina's specific features and it allows both systemic and local drug administration (1). "Macmiror Complex Vaginal Ovules" is the only approved drug containing 500 mg Nifuratel and 200.000 IU Nystatin and indicated for the treatment of vulvovaginal diseases caused by pathogenic microorganisms. As well in the most of vaginal formulations in-vivo assays cannot be performed for ovules. But also, it is impossible to show in vitro dissolution profile because of the molecules' low solubility. In this study we have aimed to investigate the solubility of Nystatin and Nifuratel in different medias to choose the best one for dissolution studies to compare the ovule formulation we will develop and the developed formulation with the reference product.

MATERIALS AND METHODS:

Solubility studies of Nystatin and Nifuratel were performed by shaking an excess amount of each drug with 2 mL of the following dissolution mediums simulated vaginal fluid(SVF), Na2HPO4 buffer pH4:0.5% sodium lauryl sulfate(SLS), Na2HPO4 buffer pH4:1% SLS, Na2HPO4 buffer pH4:methanol(ratio 60:40), Na2HPO4 buffer pH4 and methanol(ratio 40:60) (2) and acetate buffer pH4.5. The samples were incubated in 37 ℃ water bath (130rpm). After 24 hours, the samples were centrifuged at 10000rpm for 15 minutes. The supernatants were collected and injected into vials, analyzed with Schimadzu HPLC-PDA by using a Phenomenex Luna-5u column, 250mm×4.6mm and Methanol:10 mM Ammonium acetate buffer (pH 5.5) (70:30 v/v) as mobile phase with a detection wavelength of 254nm (Nifuratel(3)) and 306nm (Nystatin(4)). The method was developed, validated according to ICH guidelines.

RESULTS:

According to the results no peaks were observed for Nystatin and the lowest concentrations were observed for Nifuratel in SLS containing medias, SVF and acetate buffer. The media containing Na2HPO4 buffer pH4:methanol(40:60) showed the best result for both Nystatin and Nifuratel.

CONCLUSIONS:

It has been concluded that the best media for the former dissolution studies will be Na2HPO4 buffer pH4:methanol(40:60) containing media.

ACKNOWLEDGEMENTS:

This project is granted by Ege University, Committee of Scientific Research Project (BAP) and Aliye Üster Foundation.

REFERENCES:

1. Bernkop Schnürh A, Hornof M (2003). American Journal of Drug Delivery, 1(4): 241–254
2. Gupta J et al., (2011). Pharmacology & Pharmacy, 2: 289-298
3. Lili X et al., (2006). European Journal of Drug Metabolism and Pharmacokinetics, 32 (2): 69-73
4. Ostrosky Zeichner L et al., (2001). Antimicrobial Agents And Chemotherapy, 45(10):2781–2786.

P-293: DEVELOPMENT OF TIME CONTROLLED MULTI-COPMRESSED DEXKETOPROFEN TROMETAMOL TABLETS.

Hascicek, C., Doburlu, H., Esim, O.

Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Rheumatoid arthritis is a disease characterized by diffuse and symmetrical chronic inflammation in the joints. Morning stiffness, loss of function and severe joint pain are seen especially in the early morning hours. The adverse effects of rheumatoid arthritis at certain times have led to a focus on these hours in the treatment of the disease. For ideal therapeutic efficacy, time controlled systems design to mimic the circadian rhythm of the rheumatoid arthritis by releasing the drug at the specific time (1). The aim of this study was to develop time-controlled multi-compressed tablet formulations of dexketoprofen trometamol (DT) used in the treatment of rheumatoid arthritis and to examine the effective formulation and process parameters on the rate of drug release from tablets.

MATERIALS AND METHODS:

Multi-compressed tablets prepared containing DT in the inner core were formulated by compression-coating with ethylcellulose as the outer layer in different amount. All tablet formulations were prepared by direct compression method. Prepared tablets were evaluated for various physical parameters such as hardness, thickness, diameter, weight variation and in vitro drug release characteristics. In vitro dissolution rate studies were performed at three different pH using the USP pallet method.

RESULTS:

It has been observed that the increase in the amount of polymer in the outer layer has adversely affected the in vitro dissolution rate properties of DT. It has been determined that the increase in the compression pressure during the press-coating of the outer shell layer increases the lag time. Optimized formulation achieved a burst release of the drug from tablets after 4 h lag time.

CONCLUSIONS:

A time controlled dosage form was formulated by press coating technique. Tablet formulations exhibited two stages of release performance, a period of lag time and rapid drug release, which was mainly dependent upon the compression force and amount of the outer coating layer.

REFERENCES:

1. Straub RH, Cutolo M (2007). Arthritis & Rheumatism. 56(2):399–408

P-294: EFFECT OF POLYMER TYPE AND CONCENTRATION ON CHARACTERISTICS OF DIHYDROERGOTAMINE MESYLATE SUBLING FILMS

[1] Ozkan, CK.; [1] Esim, O.; [2] Kurbanoglu, S., [1] Savaser A.,[1] Tasi C., Arslan, A. [2] Ozkan SA., [1] Ozkan, Y.

[1]University of Health Sciences, Department of Pharmaceutical Technology, Etlik, 060[1]8 Ankara, Turkey

[2] Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

In this study, it is aimed to develop fast disintegrating sublingual film formulations containing Dihydroergotamine Mesylate (DHE) active substance and to investigate the bioavailability of those that are suitable for use in the treatment of migraine.

MATERIALS AND METHODS:

Film formulations were prepared using pullulan, maltodextrin and propylene glycol as plasticizer. Box Behnken design was used to investigate the effects of the polymer formulations on the disintegration, durability and dissolution rate of the film formulations. DHE in sublingual films were determined with HPLC coupled with florescence dedector (1).

RESULTS:

It is found that pullulan and maltodextrin concentration have significant effect on disintegration, tensile strength of sublingual films ($p<0.05$). higher pullulan concentration coused a retention in disintegration time and increased the tensile strength. The effect of polymer type on disintegration, tensile strength and dissolution was shown in Fig.1.

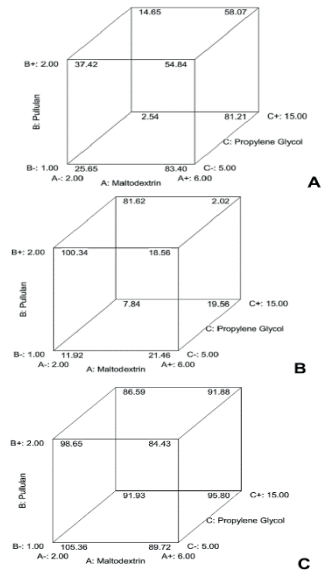


Fig.1. Effect of polymer type and concentration on disintegration (A), tensile strength (B) and mean dissolution time (C) of DHE sublingual films.

CONCLUSIONS:

According to the obtained data, it can be said that DHE sublingual films can be prepared by solvent casting method and both polymer type and concentration have a significant effect on sublingual films.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-214S655)

REFERENCES:

1. Kurbanoglu S et al.Rev. Roum. Chim 62.6-7 (2017): 517-523.

P-295: PREPARATION AND OPTIMIZATION OF CUCURBITACIN B LOADED CORE-SHELL TYPE HYBRID NANOPARTICLES USING A FULL FACTORIAL DESIGN STUDY

[1] Sengel Turk, C.T., [2] Ozmen, N., [2] Bakar Ates, F.

[1] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

[2] Ankara University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey

INTRODUCTION:

Cucurbitacin B is a triterpenoid derived natural compound which is present in plants and it's been reported that this compound has antiproliferative efficiency in various cancer cells (1). Although some drug carrier formulations loaded with cucurbitacin B have been developed (2), there is no data about the development of a new generation drug delivery system of cucurbitacin B named as core-shell type lipid-polymer hybrid nanoparticles that involved architectural advantages of biodegradable polymeric nanoparticles and biomimetric characteristics of liposomes within stable structure of a combined carrier system. In this context, the present study aimed to develope cucurbitacin B-loaded core-shell type lipid-polymer hybrid nanoparticles by one-step self-assembly approach method. A systematic screening research was employed to optimize the hybrid formulations by using a 32 full factorial design with center points.

MATERIALS AND METHODS:

Nine batches were prepared as a per 32 full factorial design to optimize the amount of DSPE-PEG/PLGA ratio (X1) and the total lipids/L-α-phosphatidylcholine molar percentage ratio (X2) investigated based on the particle size of cucurbitacin B-loaded hybrid systems. Design Expert 6.0.8 software was utilized to carry out the optimization of the system. RSM approaches and also contour and linearity plots were used to optimize the process. Encapsulation efficiency values were determined by using a HPLC validated method to evaluate the particle characteristics of the developed hybrid formulations.

RESULTS:

The particle size of the all core-shell type hybrid nanoparticles ranged from 94.5 to 127.2 nm with polidispersity in the range between 0.097-0.118 inhibited a narrow size distribution. Considering the influence of X1 and X2 on the particle size of the hybrid nanocarriers indicated that size of the core shell type hybrid particles increased as the X2 level increased at each X1 level.

CONCLUSIONS:

This research demonstrated that the particle size of the core-shell type hybrid nanoparticles loaded with cucurbitacin B could be manipulated by variation of the contents of the lipids and polymer.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-117S131)

REFERENCES:

1. Bakar F (2016). Anticancer Agents Med Chem., 16(6):747-754.
2. Wang W, Zhao X, Hu H, Chen D, Gu J, Deng Y, Sun J (2010). Drug Delivery, 17(3):114-122.

P-296: INFLUENCE OF THE LIPID MATERIAL ON PHYSICOCHEMICAL PROPERTIES OF SOLID LIPID NANOPARTICLES

Ozturk, C., Amasya, G., Tarımci, N.

Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Solid lipid nanoparticles (SLNs) which are new promising drug delivery systems for dermal application have been proven to be effective against various skin conditions. These property results from the ability of the solid lipid nanoparticles to penetrate the skin layers easily (1). SLNs which are colloidal drug delivery systems are produced with lipids in solid state at both body and room temperature such as fatty acids (e.g. stearic acid), triglycerides (e.g. tristearin), partial glycerides (e.g. glyceryl behenate) and waxes (e.g. cetly palmitate) or mixtures of them. The physcochemical properties of SLNs mostly depend on the lipid material. The purpose of the present study is to investigate the infuluence of the various type of solid lipids on the physcochemical properties of SLNs.

MATERIALS AND METHODS:

Hot homogenization method was prefered to produce SLNs. Because organic solvents can be avoided and it provides easy production. This method is carried out at temperatures above the melting point of the lipid and is similar to the homogenization of an emulsion. Three kind of lipid materials with various melting point, Compritol 888 ATO which is partial glycerides, Precirol 5 ATO consists of esters of palmitic and stearic acids and Stearic acid which is a fatty acid were used to prapere SLNs in this study. Poloxamer 188 was used as stabilizer and the SLNs were characterized according to particle size, size distribution and surface charge.

RESULTS:

When all results were evaluated, it is possible to obtain SLNs in the nanometer range with all solid

lipids successfully. It was also observed that the increment of the melting point of solid lipid has a significant effect on the particle size and the particle size has decreased, as the melting point increased. Narrow particle size distrubition was achieved by all SLN formulations and negatively high zeta potential value which shows the stability of colloidal system was obtained by Compritol 888 ATO based SLNs.

CONCLUSIONS:

Although SLNs have many advantages, drug leakage from carrier system during storage may ocur because of the crystal lattice of SLNs. The melting point of lipid is important since solid lipids may significantly decrease the mobility of the drug molecules within the lipid core and thus reduce drug leakage (2). This study has shown it is possible to obtain SLNs which has suitable physicochemical properties with a partial glyceride, Compritol 888 ATO which has relatively high melting point.

REFERENCES:

1. Escobar Chavez, et al. 2012. Nanocarrier systems for transdermal drug delivery, Sezer A.D. (Ed.), Recent Advances in Novel Drug Carrier Systems, Intech, pp. 202–240.
2. Naguib, et al. 2014. Solid Lipid Nanoparticle Formulations of Docetaxel Prepared with High Melting Point Triglycerides: In Vitro and in Vivo Evaluation, Mol. Pharmaceutics, 11, 1239−1249.

P-297: DEVELOPMENT OF A FILM FORMULATION CONTAINING DOXYCYCLINE HYCLATE FOR THE TREATMENT OF PERIODONTAL DISEASES

[1] Dayıoglu, D., [1,2] Cetin Uyanikgil, EO.

[1]Ege University, Faculty of Pharmacy, Izmir, Turkey

[2]Ege University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Department of Biopharmaceutics and Pharmacokinetics, Izmir, Turkey

INTRODUCTION:

Periodontal disease is defined as infections of the tissues surrounding and supporting the teeth. The delivery of antibacterial agents to the disease site has been carried out by systemic or topical administration (1-3). The aim of this study was to develop a controlled release formulation including doxycycline hyclate using hydrolyzed gelatin as a drug carrier material.

MATERIAL AND METHOD:

The hydrolyzed gelatin films (10%) containing 30% glycerin and 125 mg doxycycline hyclate were prepared by the solvent evaporation technique (4). These mixtures were poured on teflon plates and evaporated at 37ºC temperature 44 hours. The films were then cut in a desired form. The cut films were hardened with 10% formaldehyde solution in isopropyl alcohol for 1, 4, 8, 12 and 24 h and then washed with acetone and dried at room temperature for crosslinking. In vitro release studies were performed using a syringe pump (Kd Scientific) in pH 7.4 phosphate buffer and the flow rate was 50 ml/hour. Determinations were done spectrophotometrically (Shimadzu UV-1280) at 341 nm and the release profiles were plotted as a function of time. The thicknesses were measured from 6 different places with digital calipers and the averages were taken. The films spectra were taken with ATR FT-IR (Perkin-Elmer Spectrum 100).

RESULTS:

Doxycycline hyclate was released immediately from 10% hydrolyzed gelatin film, 1 and 4 hours hardened films. The formulations were hardened for 8, 12 and 24 hours and doxycycline hyclate was released for 3 days. The release profiles of all formulations were fitted to Higuchi kinetic model.

CONCLUSIONS:

In conclusion, doxycycline hyclate containing hydrolyzed gelatin film can be used in the treatment of periodontal disease.

ACKNOWLEDGEMENTS:

This dissertation thesis has been carried out in E.U. Faculty of Pharmacy, Department of Biopharmaceutics and Pharmacokinetics Research Laboratory.

REFERENCES:

1. Pihlstrom B et al. (2005). Lancet, 366: 1809- 20.
2. Schwach Abdellaoui K et al. (2000). E. J. Pharmaceutics and Biopharm, 50, pp. 83-89.
3. Cetin EO et al. (2005). J Clin Periodontol; 32: 773–777.
4. Cetin EO et al. (2004). J Clin Periodontol; 31: 1117–1121.

P-298: PREPARATION AND CHARACTERIZATION OF W/O/W DOUBLE EMULSION CONTAINING TENOFOVIR

Bektas, D., Tugcu Demiroz, F., Teksin ZS.

Gazi University Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Water-in-oil-in-water (w/o/w) double emulsions are able to enhance oral bioavailability of BCS Class 3 drugs with high solubility and low permeability. Tenofovir (TNF) is a BCS Class 3 drug and it has low bioavailability (1). The aim of this study was to develop double emulsion (DE) for TNF and characterization of TNF-DE.

MATERIALS AND METHODS:

Tenofovir was obtained as a gift sample from Pharmactive Ltd, Turkey. Imwitor 742 was obtained from IOI Oleo GmbH, Germany. Solubility of TNF was determined in imwitor 742, abilem-90, labrafil M1944 CS, and propylene glycol by shake flask method (24 hours, 37±0,5°C). Double emulsions are prepared by a modified two-step emulsification method, using imwitor 742 (oil phase), labrafil M 1944 CS, propylene glycol (hydrophilic emulsifier) and abilem-90 (hydrophobic emulsifier).The droplet sizes, polydispersity index (PDI), zeta potential, turbidity, and viscosity was measured and evaluated characterization for TNF-DE. Double emulsion was analyzed under polarized light microscope. The in vitro release studies of TNF-DE was performed in USP Apparatus II. The TNF-DE formulation was put in hard gelatin capsules (00, Coni-snap®). TNF was quantified by UV validated spectrophotometric method (2).

RESULTS:

The solubility of TNF in imwitor 742, abilem-90, labrafil M1944 CS, propylene glycol is 64.4± 0.007 mg/mL, 84.3±0.05 mg/mL,105.1±0.06 mg/mL,172.7±0.02 mg/mL, respectively. The droplet sizes of developed primary emulsion and double emulsion were 126.3±4.79 nm and 1459±58.39 nm and then PDI values of 0.053±0.046 and 0.74±0.08, respectively. The zeta potential and turbidity values of TNF-DE were −3.39±0.32 and 31.3±0.153 and the viscosity value was 54.66±0.58cp in 40 rpm. It was observed with a polarized light microscope(40x) that the emulsion was of multiple character. The percentage of TNF released was over 85% within 30 minutes for pH 1.2, pH 4.5 and pH 6.8.

CONCLUSIONS:

In this study, w/o/w emulsion containing TNF was successfully developed by a modified two-step emulsification process. In vitro release and characterization studies showed that w/o/w emulsion could be potential as a new oral delivery system for TNF. Furthermore, the bioavailability study will be conducted to compare in vivo performance of TNF-DE with the commercial product in future.

ACKNOWLEDGEMENTS:

This study was supported by TUBITAK, project number: 155S405.

REFERENCES:

1. Kearney B et al. (2004). ClinPharmacokinet., 43(9), 595-612
2. Bektas D et al. (2017). 2nd International Gazi Pharma Symposium Series, Ankara, Turkey.

P-299: EFFECT OF SOLVENT RATE MIXTURES ON THE RUTIN RELEASE RATE FROM POLY-E-CAPROLACTONE NANOPARTICLES

[1] Gecgel, DS., [2] Yazeji, T., [2] Lamprecht, A. [2, 1] Kilicarslan, M.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

[2] University of Bonn, Department of Pharmaceutics, Bonn, Germany

INTRODUCTION:

Rutin is a herbal flavonoid with prominent pharmacological activities such as anti-inflammatory, anti-oxidant and anti-asthmatic properties (1,2). However, its bioavailability is poor due to its low aqueous solubility (3-5). In this study, rutin nanoparticles were prepared and effect of the rate of the solvents used in formulation on the release rate was investigated.

MATERIALS AND METHODS:

Rutin nanoparticles were prepared using o/w solvent evaporation method. The polymer poly-ε-caprolactone was dissolved in dichloromethane and rutin was dissolved in methanol, by varying the solvent ratios (1:1, 1:3 and 1:5). The solutions were mixed and emulsified in the aqueous phase containing 0.3% polyvinyl alcohol. The emulsion was sonicated and the solvents were removed by evaporation. Particles were analyzed for their size and Zeta potential. Drug entrapment efficiency was determined in the supernatant. In vitro released drug amount was determined by UV spectroscopy. Release study was performed by dialysis membrane method in pH 7.4 phosphate buffer solution at 37ºC with 50 rpm by shaker.

RESULTS:

Optimum formulation had the rate of 1:3 with a particle size of 275 ± 22 nm and Zeta potential -13.0 ± 0.2 mV. Entrapment efficiency was 95.0% ± 0.3 and the release rate was 88.67% ± 12.72 in 48 h, unlike from pure rutin solution which had a release rate of 20.31% ± 2.63 in 48 h (Figure 1).

CONCLUSIONS:

In our study, it was shown that rutin nanoparticles could be formulated and dissolution rate of the drug was increased clearly. It was observed that, when methanol amount in the formulation was decreased, the release rate of rutin was decreased due to its declined solubility degree in methanol.

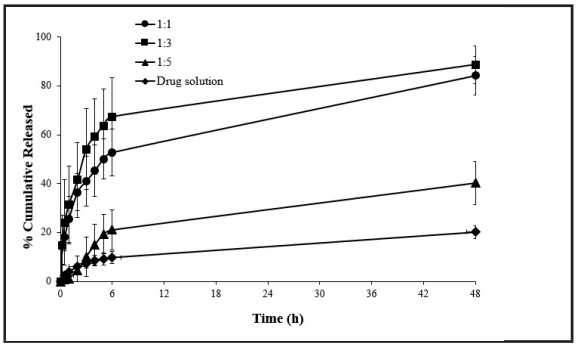


Figure 1. Release rates of rutin and rutin nanoparticles with different solvent rates (n=3).

REFERENCES:

1. Chua LS (2013). J Ethnopharmacol, 150:805-817.
2. Jung et al., (2007). Arch Pharm Res, 30:1599-1607.
3. Mauludin et al., (2009). Int J Pharm, 370:202-209.
4. Rabišková et al., (2012). Int J Pharm, 422:151-159.
5. Gullón et al., (2017). Trends Food Sci Technol, 67:220-235.

P-300: MECHANICAL PROPERTIES AND EX-VIVO SKIN PERMEATION EVALUATIONS OF IBUPROFEN EMULSION GEL FOR TOPICAL DELIVERY

Yilmaz Usta, D., Tugcu Demiroz, F., Teksin, ZS.

Gazi University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Ibuprofen (IBU) is commonly used for the treatment of pain, fever, rheumatoid arthritis and osteoarthritis. However, it is a BCS 2 drug which is poorly water-soluble, which may affect its absorption and therapeutic effects (1). Because of its poor skin permeability, it is difficult to obtain an effective therapeutic concentration from topical preparations (2). The aim of this study was to evaluate the mechanical properties, mucoadhesive value and ex vivo rabbit skin permeability of IBU emulsion gel for topical delivery.

MATERIALS AND METHODS:

Carbopol®974 and Carbopol®934 were purchased from Noveon, Parkoteks Chemical, Turkey. IBU was supplied from Sanovel, Turkey. In this study, four different ibuprofen emulsion gel (F1, F2, F3, and F4) were prepared with isopropanol, Tween 80, propylene glycol, isopropyl myristate, ethanol, Carbopol®974 or Carbopol®934. IBU emulsion gel were prepared by mixing and homogenising an oil phase and a water phase to contain 5% IBU. Their viscosity, mechanical properties (back extrusion test and spreadability test) and mucoadhesive value were assessed with a Brookfield Rheometer and TA.XTplusTexture Analyzer (Stable MicroSystems, Godalming,U.K) for topical delivery. Moreover, their skin permeation was evaluated using Franz diffusion cell with the hairless rabbit skin. These tests were performed according to the methods used in our previous study (3). All experiments were repeated in the commercial hydrogel (Neoprofen Gel® (N), Pensa Drug, Turkey) for comparison purposes. Neoprofen was a 5% IBU hydrogel prepared with carbopol as a base.

RESULTS:

The viscosity of all formulations was found suitable for topical application. Formulation F3 gave significantly higher firmness and work of shear cohesiveness than the commercial hydrogel (140±5 g vs. 417±8g; 78,3±4 g.sec vs. 311±12 g.sec). It was found the excellent mechanical properties compared to the commercial hydrogel. The work of mucoadhesion of the formulation F3 to the rabbit skin is about three times that of the commercial hydrogel (F3: 0.100±0.276, N: 0.041±0.215 mJ/cm2). IBU emulsion gel gave a significant higher permeability coefficient of about 1.4 fold compared to the commercial hydrogel. Thus, the IBU emulsion gel improved the skin permeability.

CONCLUSIONS:

In conclusion, the F3 emulsion gel formulation with good mechanical properties, mucoadhesive properties and good skin permeation would be an alternative candidate for topical delivery.

ACKNOWLEDGEMENTS:

The authors would like to thank Sanovel for providing Ibuprofen.

REFERENCES:

1. Liu Y (2018). AAPS PharmSciTech., 19(1):338-347
2. Irvine J (2018). Drug Dev Ind Pharm., 44(2):173-183
3. Tugcu Demiroz F (2017). Chem. Pharm. Bull., 65: 660–667.

P-301: DEVELOPMENT AND CHARACTERIZATION OF NANOEMULSIONS CONTAINING SILYMARIN FOR COSMETIC PURPOSES

Altuntas, E., Yener, G., Akar, E.

Istanbul University, Department of Pharmaceutical Technology, Istanbul, Turkey

INTRODUCTION:

Silymarin is a polyphenolic flavonoid obtained from seeds of the milk thistle which is of great interest to protect skin against UV radiation (1). Recent studies showed that silymarin constituents could strongly protect against photocarcinogenesis and inhibit skin inflammation and edema (2,3,4). It is reported that the main component of silymarin, silibinin, has a low skin tissue distribution by oral administration in mice (5). For this purpose, we aimed to develop a silymarin nanoemulsion in order to benefit from the anti-aging potantial of silymarin sufficiently.

MATERIALS AND METHODS:

Silymarin (0.2%, 0.5%, 1% w/w) (Sigma-Aldrich, USA) laden topical nanoemulsions were prepared using Pluronic® F-68 (Sigma-Aldrich, USA) (15% w/w) as a surfactant and Transcutol® P (Gattefossé, France) (20% w/w) as a cosurfactant by ultrasonication method. Sonication process was carried out for different emulsification time (10, 15, 20, and 30 min, in which each cycle consisted of 30 s pulses on and 30 s pulses off). Subsequently, nanoemulsions were characterized according to their mean droplet size, zeta potential, pH, conductivity, viscosity, and stability. In order to evaluate the stability, firstly, centrifugation test and thermal stress test were conducted. Suitable formulations were then subjected to heating-cooling test (six cycles) and physicochemical stability tests for 3 months. The in vitro release of silymarin was also evaluated.

RESULTS:

The formulation composition containing 1% w/w silymarin and 4% w/w oily phase was selected as the optimized formulation with a 20 minute sonication time. The optimized nanoemulsion demonstrated a nanometric particle size of 287,6±0,5 nm, a PDI of 0,257, a negative zeta potential of -34,1±0,6 mV, a pH value of 5.63, and a conductivity value of 50.5 µs/cm. Comparative in-vitro release study showed the ability of the nanoemulsion to significantly enhance silymarin release (98.4% drug release after 6 h) compared with conventional emulsion (only 54.7% drug released after 6 h).

CONCLUSIONS:

The studied nanoemulsion enhanced silymarin release while maintaining adequate physical and chemical stability. The use of silymarin laden nanoemulsion via topical skin route may provide an effective strategy for mitigating the adverse biological effects of solar UV radiation.

ACKNOWLEDGEMENTS:

This study was supported by Scientific Research Project Coordination Unit of Istanbul University (Project Number: 53854)

REFERENCES:

1. Hung C, Lin Y et al., (2010). Acta Pharmacologica Sinica, 31:118–126.
2. Meeran SM, Katiyar S et al., (2006). Mol Cancer Ther, 5:1660–8.
3. Yang B, Kotani A et al., (2001). Anal Sci, 17:599–604.
4. Zielińska-Przyjemska M, Wiktorowicz K (2006). Phytother Res, 20:115–9.
5. Zhao J, Agarwal R (1999). Carcinogenesis, 20:2101–8.

P-302: EVALUATION OF IN VITRO EFFECTIVENESS OF NANOEMULSIONS CONTAINING PIPERINE FOR THE TREATMENT OF VITILIGO DISEASE

[1] Ozkan B., [1] Budama Kilinc, Y., [1] Cakir Koc, R., [1] Kaya, Z., [2] Altuntas, E.

[1] Bioengineering Department, Yildiz Technical University, İstanbul, Turkey

[2] Pharmaceutical Technology Department, İstanbul University, İstanbul, Turkey

INTRODUCTION:

Leukoderma, also known as vitiligo, is a chronic skin disease occurs as a result of pigment loss that causes irregular distribution of pigment in the skin. Especially in the body areas exposed to the sun, pigment gradually fades and causes visible color change(1). Nowadays, the methods that are used in treatment are known to have many side effects in the long term and are not always efficient(2). Stimulants that increase the melanocyte proliferation are a potential teratment type for skin diseases like vitiligo. Piperine, an alkaloid obtained from pepper (Piper nigrum L.). Its synthetic derivatives can stimulate pigmentation in the skin and has shown appreciable capacity to repigment skin. In this study, it was aimed to produce a piperine nanomemulsion for topical use of the formulation in the treatment of vitiligo disease.

MATERIALS AND METHODS:

After the preparation of the nanoemulsions, their physico-chemical stability tests and characterization studies were carried out. Then, in vitro cytotoxicity experiments were performed with XTT assay. Finally, stimulation of melanin production by nanoemulsions were analyzed by in vitro experiments on Melanoma B16 cell line.

RESULTS:

According to data obtained from thermal stress, centrifugation tests and droplet size analyzes; two nanoemulsion formulations were found stable and they were used for in vitro experiments.

CONCLUSIONS:

Using nanoemulsions in treatment of diseases can provide several advantages such as creating a large surface area due to having small droplet size, increasing the rapid and deep penetration of the reagents into the skin and having high stability. In this study, the physicochemical stability, cytotoxicity, melanin content of piperine loaded nanoemulsions were evaluated.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Yildiz Technical University Scientific Research Projects Coordination Department (Project No. FKG-2017-306).

REFERENCES:

1. Thambirajah R (2009). Cosmetic Acupuncture, 97-135.
2. Lakhani DM, Deshpande AS (2014). Journal of Applied Pharmaceutical Science, 4 (11), 101-105.

P-304: PREPARATION OF SIO2 DOPED BIODEGRADABLE POLYACRYLIC ACID NANOCOMPOSITE HYDROGELS FOR UPGRADING OF LIFE UNDER WATER

Gokmen, F.O., Yaman, E., Temel, S.

Bilecik Seyh Edebali University, Central Research Laboratory, Bilecik, Turkey

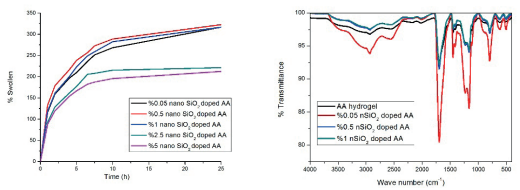
INTRODUCTION:

Because of their well swelling behavior, synthesized nanocomposite hydrogels were used as a super adsorbent (1). Aim of this study is production of nanocomposite hydrogels to upgrade of aquatic organisms' living area.

MATERIALS AND METHODS:

In this study, a biodegradable super adsorbent nanocomposite hydrogel was synthesized by in-situ free radical polymerization technique.

RESULTS:



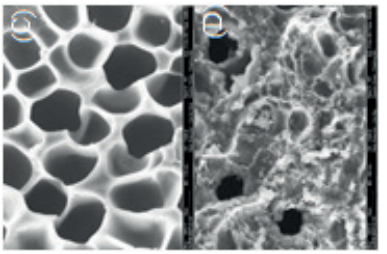


Fig.2. Fig.1. Swelling Behavior (A), FT-IR spectrums (B), SEM images of undoped (C) and doped (D) hydrogels

CONCLUSIONS:

The results of this study showed that, the increase of nano SiO2 doping causes the decrease of hydrogel porosity. Thus the adsorption studies can be chosen as superadsorbents for improve of life under water.

ACKNOWLEDGEMENTS:

This work was supported by Scientific Research Project Commission of Bilecik Seyh Edebali University (project number is 2017-01.BŞEÜ.28-01).

REFERENCES

1. Gaharwar AK, Peppas NA, Khademhosseini A, (2014), Biotehcnology and Bioengineering, 111(3): 441-453.

P-305: BIOCOMPATIBLE TIO2 DOPED HYDROGEL PRODUCTION FOR DRUG DELIVERY SYSTEMS

[1] Gokmen, FO., [1] Yaman, E., [1] Temel, S., [2] Ozbay, N.

[1]Bilecik Seyh Edebali University, Central Research Laboratory, Bilecik, Turkey

[2]Bilecik Seyh Edebali University, Chemical Engineering Department, Bilecik, Turkey

INTRODUCTION:

Smart drug-delivery system has a significant role in the treatment of various diseases. Nowadays, with the advance of material science, particles, hydrogels and insert films have been designed and prepared to be drug carriers. TiO2 doped biodegradable hydrogels that can form gels in situ have been widely utilized for biomedical applications, such as cell/drug delivery as well as tissue engineering (1).

MATERIALS AND METHODS:

A biocompatible composite hydrogel was synthesized by in situ free radical polymerization technique. TiO2 was commercially purchased and used as a reinforcing material into composite hydrogel varying mass ratio of 0.05%, 0.5% and 1%.

RESULTS:

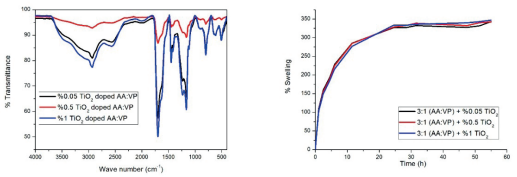


Fig.1. Swelling behavior and FT-IR spectrums of TiO2 doped AA-co-VP composite hydrogels

CONCLUSIONS:

Swelling behavior and structural properties of obtained hydrogels were specified to determine drug delivery properties.

ACKNOWLEDGEMENTS:

This work was supported by Scientific Research Project Commission of Bilecik Seyh Edebali University (project number is 2017-01.BŞEÜ.28-01). Characterizations were performed in Bilecik Seyh Edebali University Central Research Laboratory.

REFERENCES

1. Holban AM, Grumezescu AM, (2016). Nanoarchitectonics for Smart Delivery and Drug Targeting, William Andrew.

P-307: INVESTIGATION OF RIBOFLAVIN AND RIBOFLAVIN-5-PHOSPHATE SODIUM RELEASE FROM OCULAR HYDROGELS

Aytekin, E., Bozdag Pehlivan, S., Calis,S.

Hacettepe University, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Riboflavin is a vitamin that can be used as photosensitizer for collagen crosslinking procedure which is a method for stopping progression of keratoconus disease (1). Thermosensitive hydrogels can be defined as thermally induced reversible gel forming systems that can absorb high amount of water in their three dimensional structure (2). The aim of this study is to evaluate drug release from thermosensitive hydrogels containing Riboflavin or Riboflavin-5-Phosphate Sodium.

MATERIALS AND METHODS:

Thermosensitive hydrogel formulations were prepared by cold method (2). The formulations consisted of 0.1% (w/v) Riboflavin (RB coded formulations) or 0.1% (w/v) Riboflavin-5-Phosphate Sodium (RS coded formulations), Pluronic F-128, NaCl, Benzalkonium Chloride, without (RB coded formulations or RS coded formulations) or with (RB+T coded formulations or RS+T coded formulations) Transcutol P. In vitro release studies were performed using in vitro dialysis bag method (dialysis tubing 14.000 MWCO) with pH 7.4 phosphate buffer at 32oC by using Memmert Shaking Bath (WNB 7, Germany) at 100 rpm. Samples were collected at 15 min, 30 min, 1 hour, 2 hours, 6 hours, 24 hours and 48 hours. Then, the samples were analyzed with validated HPLC method for drug content. All experiments carried out in triplicate.

RESULTS:

In vitro release studies showed that 86.7±0.6% or 89.3±0.9% of Riboflavin-5-Phosphate Sodium were released from RS coded formulations or RS+T coded formulations, respectively, at the end of 24 hours. Furthermore, 67.6±1.1% or 58.7±1.6 % Riboflavin were released from RB coded formulations or RB+T coded formulations, respectively, at the end of 48 hours.

CONCLUSIONS:

It could be concluded that the developed formulations were promising for the treatment of keratoconus as they provided sustained Riboflavin or Riboflavin-5-Phosphate Sodium release.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-215S685)

REFERENCES:

1. Wollensak et al. (2003). American Journal of Ophthalmology, 135(5), 620-627.
2. Aytekin E, Bozdağ Pehlivan S, Çalış S. (2017), 2nd International Gazi Pharma Symposium Series (GPSS 2017), Ankara, Turkey, October 11-13, 2017.

P-308: DETERMINATION OF CYTOTOXICITY OF LAMOTRIGINE ON L929 CELL LINE.

[1,2] Pezik, E., [2] Oztürk, N., [2] Sahin, S., [2] Vural, I.

[1] Hacettepe University, Department of Pharmaceutical Technology, Ankara, Turkey

[2] Erzincan University, Department of Pharmaceutical Technology, Erzincan, Turkey

INTRODUCTION:

Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures (1). Lamotrigine (LTG) is a phenyltriazine derivative compound and is used as an antiepileptic agent (2). In this study, we aimed to investigate the cytotoxicity of LTG on the L929 cell line, which is derived from normal subcutaneous connective tissue of an adult mouse.

MATERIALS AND METHODS:

L929 cells were cultured in Dulbecco's Modified Eagle's Medium (DMEM) and seeded at a density of 50,000 cells / mL (5000 cells in per well) in a 96-well plate. Seven different concentrations of LTG were applied to the L929 cells. LTG stock solutions were prepared in dimethyl sulfoxide (DMSO) and dilutions

were prepared using complete medium. Maximum DMSO concentration applied to cells was 0.28 %. Cell viability was evaluated by MTT assay after 24 h and 48 h incubation with LTG dilutions.

RESULTS:

Cell viability of L929 cells after 24 h incubation were 99.4, 104.9, 106.1, 130.1, 123.9, 116.5, 121.3 % for 2, 4, 6, 8,10, 12, 14 µg/mL of LTG concentrations, respectively. After 48 h incubation cell viability values of the L929 cells were determined as 95.0, 102.5, 99.8, 149.3,221.2, 156.9 and 161.8 % at the same concentrations.

CONCLUSIONS:

It was found that LTG had proliferative effects on the L929 cells at both low and high concentrations. As a result of this study, we may conclude that LTG does not have a cytotoxic effect on the L929 cell line.

REFERENCES:

1. Fisher R. S.,et al. (2014). Epilepsia,55(4):475–482.
2. Leng Y.,et al.(2013). International Journal of Neuropsychopharmacology, 16: 607–620.

P-309: POLY-LACTIC-CO-GLYCOLIC ACID NANOPARTICLES CONTAINING KETOPROFEN LYSINE: PREPARATION AND CHARACTERIZATION

Elmaskaya, A., Özturk, AA., Yenilmez, E.

Anadolu University, Faculty of Pharmacy, Depart. of Pharmaceutical Technology, Eskisehir, Turkey

INTRODUCTION:

Ketoprofen lysine (KL), the water soluble lysine salt of Ketoprofen, is one of the most widely used non-steroidal anti-inflammatory drugs (NSAIDs) in the symptomatic treatment of various chronic inflammatory diseases for its analgesic efficacy (1). However, due to its short half-life of 1–2 h, a multiple dose regimen is required therefore, KL is an ideal candidate for the development of controlled drug delivery systems which are able to release the drug at a desired rate and in desired amount (1). PLGA exhibits many of the ideal properties of a nanoscale delivery system, providing long term release of the encapsulated agent and degrading into the biocompatible products of lactic and glycolic acid (2). According to the aim of this study, KL-containing PLGA nanoparticles were prepared by spray drying method (2).

MATERIALS AND METHODS:

KL is kind gift from Berko İlaç (Istanbul/Turkey). PLGA (Resomer® RG 504, PLGA 50:50) was obtained from Sigma(Germany). Formulations were prepared by spray drying method with Büchi B-290 spray dryer (Switzerland). Particle size (PS), poly dispersity index (PDI) and zeta potential (ZP) measurements were performed on freshly prepared samples using a Malvern analyzer. The entrapment efficiency (EE%) and dissolution study of each formulation was performed with HPLC. In vitro release study of the formulations was investigated over 15 days and performed in phosphate buffer (pH 7.4). Results:

Figure 1. In vitro dissolution profile of formulations and pure KL

Table 1. Result of PS, PDI, ZP and EE% (n=3)

CONCLUSIONS:

According to the characterization and dissolution studies we can conclude that this polymeric system seems to be promising for controlled and sustained delivery of KL for pain treatment.

ACKNOWLEDGEMENTS:

This study was supported by Anadolu University Scientific Research Project No: 1708S471

Figure 1. In vitro dissolution profile of formulations and pure KL

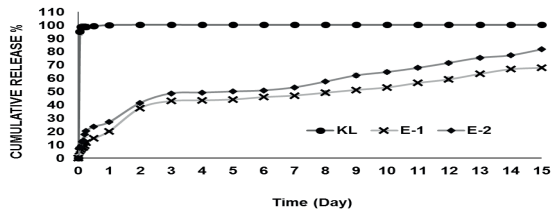


Table 1. Result of PS, PDI, ZP and EE% (n=3)

Code	Particle Size	PDI	Zeta	%EE
S-Blank	490.3 ± 2.2	0,27± 002	-28±0.21	-
S-1	512.6 ± 5.2	0.43±0.03	-27±1.13	%78.789±0.953
S-2	518.3 ± 3.1	0.44±0.02	-20±1.21	%59.634±1.624

REFERENCES:

1. Cimini, Annamaria, et al. (2015). Journal of cellular physiology 230.4 (2015): 813-820.
2. McCall, R. L., & Sirianni, R. W. (2013). Journal of visualized experiments: JoVE, (82).

P-310: PREPARATION AND CHARACTERIZATION OF KETOCONAZOLE AND CAFFEINE LOADED SELF-NANOEMULSIFYING DRUG DELIVERY SYSTEMS

[1] Gulpinar E., [2] Tirnaksiz F.

[1]Ezgi Gulpinar Pharmacy, Ankara, Turkey

[2]Gazi University, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Ketoconazole (KET) and caffeine (CAF) are known as active molecules which provide their effects via hair follicles on the scalp. Topical KET is used for treatment of seborrhoeic dermatitis (SD) and dandruff. The topical using of its shampoo was also reported to be effective against androgenetic alopecia. It can be useful for treating SD accompanied by hair regression. Caffeine has potent antioxidant properties and increases microcirculation in the skin; and also stimulates hair growth. Unfortunately, limited penetration through the skin of these components causes decreasing of their therapeutic effects. The follicular route is important for targeted delivery of the topical drugs to pilosebaceous unit and nanoemulsions can increase penetration of topical drugs through transfollicular pathway.

The aim of this study is to develop and characterize of a new self-nanoemulsifying delivery system which contains ketoconazole in inner oil phase and caffeine in outer aqueous phase.

MATERIALS AND METHODS:

- Ketoconazole
- Caffeine
- Cremophor RH40
- Transcutol P
- Miglyol 818
- Argan oil
- Construction of Ternary Phase Diagrams,
- Preparation of Formulations;
- Characterization of Formulations;
- Droplet size and pDı measurement;
- Dilution Test;
- Viscosity and Flow Properties Determination;
- Surface Tension Measurement;
- Ostwald Ripening Measurements;

RESULTS:

The appropriate carrier system was composed of Cremophor RH40, Transcutol P, the mixture of argan oil-mglyol 818 and distilled water. The mean droplet size and polidispersity index of self-nanoemulsion system was determined as 23.50 nm and 0.247, respectively.

CONCLUSION:

Our in-vitro system parameters represented that the KET and CAf loaded self-nanoemulsion system could be promising to use topically for the treatment of some hair loss pathologies.

REFERENCES:

1. Hugo Perez BS. Ketocazole as an adjunct to finasteride in the treatment of androgenetic alopecia in men California College of Podiatric Medicine San Francisco, USA
2. N. Otberga A, Teichmanna U, Rasuljevb R, Sinkgravena W, Sterrya J, Lademanna
3. Follicular Penetration of Topically Applied Caffeine via a Shampoo Formulation

P-311: OPTIMIZATION OF POLY (ACRYLIC ACID-CO-N-VINYL 2-PYRROLIDONE) / SIO2 NANOCOMPOSITE HYDROGELS FOR DRUG DELIVERY SYSTEMS

Gokmen, FO., Temel, S., Yaman, E.

Bilecik Seyh Edebali University, Central Research Laboratory, Bilecik, Turkey

INTRODUCTION:

The unique properties of hydrogels, including the ability to change from solution to solid form, make them excellent platforms for localized drug delivery applications (1). Aim of this study, to obtain best hydrogel to release drug into human body.

MATERIALS AND METHODS:

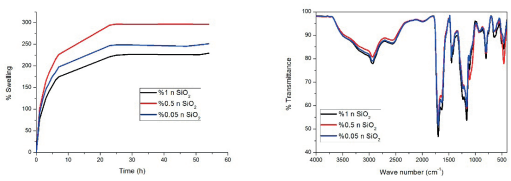
Acrylic acid and N-vinyl 2-pyrrolidone were used in this study to synthesized nano SiO2 based copolymeric nanocomposite hydrogels.

RESULTS:

Table.1. %C and %CL values of AA-co-VP nanocomposite hydrogels

AA-co-VP/nSiO2 ratio	%C	%CL
%1 n SiO2	85.06	94
%o.5 n SiO2	84	93
%0.05 n SiO2	93	92

Fig.1. Swelling behavior and FT-IR spectrums of AA-co-VP nanocomposite hydrogels



CONCLUSIONS:

Swelling behavior of nanocomposite hydrogels were calculated to find % conversion (%C), % crosslinking (%CL) and % swelling (%S) values. The chemical structures of the hydrogels were measured by FT-IR analysis.

ACKNOWLEDGEMENTS:

This work was supported by Scientific Research Project Commission of Bilecik Seyh Edebali University (project number is 2017-01.BŞEÜ.28-01).

REFERENCES

1. Holban AM, Grumezescu AM (2016). Nanoarchitectonics for Smart Delivery and Drug Targeting, William Andrew.

P-312: PREPARATION, CHARACTERIZATION AND SWELLING BEHAVIOR OF PAA/PVP COPOLYMERIC HYDROGEL AS A DRUG CARRIER AGENT

[1] Gokmen, FO., [1] Temel, S., [1] Yaman, E., [2] Ozbay, N.

[1]Bilecik Seyh Edebali University, Central Research Laboratory, Bilecik, Turkey

[2]Bilecik Seyh Edebali University, Chemical Engineering Department, Bilecik, Turkey

INTRODUCTION:

Hydrogels are 3-D polymer networks capable of swelling in water or biological liquids, and retaining a large amount of liquids in the swollen state (1).

MATERIALS AND METHODS:

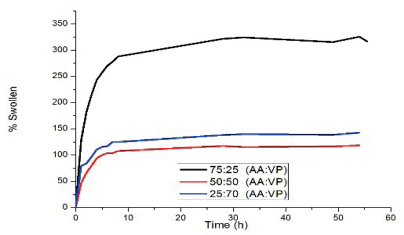
In this study, free radical polymerization technique was chosen for production. Acrylic acid and Vinyl pyrrolidone were used as monomers in solution due to their biodegradability to perform as a drug carrier agent.

RESULTS:

Table.1. %C and %CL values of AA-co-VP copolymeric hydrogels

AA:VP ratio	%C	%CL
75:25	95.50	81.34
50:50	104	74.76
25:75	91.83	63.16

Fig.1. Swelling behavior of AA-co-VP copolymeric hydrogels



CONCLUSIONS:

Acrylic acid hydrogels were obtained in the presence of a radicalic initiator. Acrylic acid and vinyl pyrrolidone polymers obtained under optimum conditions were synthesized by free radical polymerization method using crosslinking agent. % Conversion (%C), % crosslinking (%CL) and % swelling (%S) values of the hydrogels were calculated.

ACKNOWLEDGEMENTS:

This work was supported by Scientific Research Project Commission of Bilecik Seyh Edebali University (project number is 2017-01.BŞEÜ.28-01). Characterizations were performed in Bilecik Seyh Edebali University Central Research Laboratory.

REFERENCES

1. Gokmen FO, Pekel Bayramgil N (2017). Eur. Chem. Bull., 6(11):514-518.

P-313: EVALUATION OF INTRAVAGINAL DELIVERY OF POLYVINYLPYRROLIDONE-METRONIDAZOLE NANOFIBERS FOR THE TREATMENT OF BACTERIAL VAGINOSIS

Tugcu Demiroz, F., Saar, S., Tort, S., Kara, AA., Acartürk, F.

Gazi University, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Bacterial vaginosis (BV) is one of the most common genital conditions occurring in women. BV, when treated, is generally managed by using metronidazole (MTZ), which belongs to the nitro-imidazole class of antibiotics and exhibits broad spectrum activity against most gram-negative and gram-positive anaerobic bacteria (1). Nanofibers offer many advantages for vaginal drug delivery, including high loading and encapsulation efficiency and relatively prolonged residence time (2). The aims of this study were to develop mucoadhesive nanofibers containing metronidazole via electrospinning method and to characterize them for the treatment of BV.

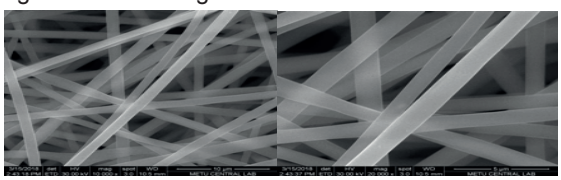
MATERIALS AND METHODS:

Polyvinylpyrolidone (PVP) solutions were prepared in the concentration of 10, 12,5 and 15% (w/v) in ethanol and the nanofibers were produced by electrospinning method. The MTZ loaded polymer solution at different PVP concentrations were compared in terms of viscosity, conductivity and surface tension. MTZ nanofibers were characterized by fourier transform infrared spectroscopy (FTIR), differential scanning calorimetry (DSC) and scanning electron microscopy (SEM). Drug loading and mechanical properties of MTZ nanofibers were also investigated.

RESULTS:

An increase in the polymer concentration from 10 to 15 % led to a decrease in the solution conductivity and surface tension values and an increase in the viscosity values for both polymer solutions and MTZ-loaded polymer solutions. DSC and FT-IR analyses indicate that there were no interactions between MTZ and PVP. The mean diameters of the MTZ nanofibers were found to be 955, 1344 and 2385 nm for PVP concentrations of 10, 12,5 and 15 %, respectively. The MTZ nanofibers were found very hydrophilic with contact angle values of 0°. Tensile strength and elongation at break values increased from 2,91 to 5,36 MPa and from 28 to 32 % for PVP concentrations between 10-15%, respectively. Entrapment efficiency of MTZ in the nanofiber mats was found to be 50, 66 and 63 µg/cm2 for PVP concentrations of 10, 12,5 and 15 %, respectively. SEM images show that homogeneous structure was observed for PVP-MTZ nanofibers (Fig 1).

Figure 1. SEM images of PVP-MTZ nanofiber



CONCLUSIONS:

In the present study, we successfully developed MTZ incorporated PVP nanofibers for the treatment of BV. PVP nanofibers incorporating MTZ are potentially capable of eradicating in vivo one of the principal microorganisms implicated in the pathogenesis of BV.

REFERENCE

1. Pathak M et al., (2014). Journal of Biomaterial Applications 29(3):354-63
2. Krogstad EA et al., (2017). Biomaterials, 144:1-16.

P-314: DEVELOPMENT AND EVALUATION OF EXTENDED RELEASE TABLET FORMULATIONS OF VENLAFAXINE HYDROCHLORIDE

Saar, S., Yıldız A., Unal, IS., Ozdal, ZD., Olgac, S., Kodan, E., Duran, C., Tort S., Tugcu Demiroz, F.

[1] Gazi University, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Venlafaxine hydrochloride(VH), an antidepressant, is used in treatment of major depressive disorder, social anxiety disorder and panic disorder(1). The half-life of VH following immediate release formulations is 5±2 h. Therefore, immediate release VH formulations must be given two or three times to maintain adequate plasma drug concentration(2). The aim of present study was to develop VH extended release tablets to be given once daily which have dissolution profile similar to commercial VH extended release tablets.

MATERIALS AND METHODS:

VH extended release tablets were prepared by direct compression method(Table 1). The powders of formulations were evaluated for angle of repose, flow rate, Carr's index and Hausner ratio. The prepared tablets were characterized for weight variation, hardness, friability and in-vitro drug release studies. The in-vitro drug release was studied in two different pH media (2h at pH 1,2 and then 10h at pH 6,8) using USP apparatus I. The difference factor(f1) and similarity factor(f2) were calculated for all formulations and similarity of the tested commercial tablet was determined.

RESULTS:

The angle of repose, flow rate, Carr's index and Hausner ratio of powder formulations were given in Table 1. The results of the powder characterization obtained for powders were taken as an indication of good compressibility of tablets. The friability values were less than 1% within the acceptable limits for all formulations. Hardness of the tablet formulations were found to be between 43-142N. Based on the in-vitro dissolution studies, the drug release from F1 was found similar as compared to the commercial tablets. The f1 and f2 factors for F1 with reference commercial tablets were 15,09 and 54,49 respectively.

Table 1. Composition of formulations and characterization of powders

Formulation Code Ingredients(mg)	F1	F2	F3	F4
Venlafaxine hydrochloride	84,85	84,85	84,85	84,85
Avicel PH-102	115	115	115	115
Aerosil200	5	5	5	5
Magnesium Stearate	5	5	5	5
Carbapol974	20	-	-	-
HPMC K100M	120	-	-	-
Polyethylene oxide(PolyoxWSR303)	-	140	-	-
Guar Gum(SupercolNF)	-	-	140	-
Alginate(ProtanalLF240)	-	-	-	140
POWDER CHARACTERIZATIONS				
Angle of Repose(°)	28,9±3,19	28,8±1,91	32,1±5,57	56,75±7,96
Flow Rate(g/s)	35,1±7,12	4,3±0,27	3,8±1,3	33,02±3,26
Carr's Index(%)	17,5	13,2	21,42	16,67
Hausner Ratio	1,21	1,15	1,27	1,20

CONCLUSIONS:

VH extended release tablets were successfully prepared by direct compression method. It was shown that the release profile of F1 was similar to the commercial tablet. Thus, results of the current

study clearly indicate a promising potential of the venlafaxine hydrochloride extended release tablet as an alternative to the conventional tablet.

REFERENCES:

1. Feighner JP., (1994). J Clin Psychiatry, 55:98-100.
2. Krishna KV. et al., (2014). Int J Sci Res Pub, 4(10):1-20.

P-315: METRONIDAZOLE INCORPORATED POLYMERIC NANOPARTICLES FOR VAGINAL APPLICATION

[1] Katerji, F., [2] Basaran, E.

[1]Anadolu University, Institute of Health Sciences, Eskisehir, Turkey

[2]Anadolu University, Department of Pharmaceutical Technology, Eskisehir, Turkey

INTRODUCTION:

Despite being so effective on many bacterial infections, Metronidazole (MET) showed many side effects when administered orally in a number of patients which may necessitate its withdrawal from therapy (1). In our study for the avoidance of proposed side effects, preliminary studies on novel formulations were developed for the vaginal application of MET.

MATERIALS AND METHODS:

Metronidazole and Kollidon® SR (KSR) were kindly gifted by Haver Ilac (Istanbul, Turkey) and BASF (Istanbul, Turkey) respectively. Tween® 80 (T80) was obtained from Merck (Hohenbrunn, Germany). All other chemicals were in analytical grade.

Nanoparticles were prepared by emulsification-solvent evaporation method (2). In vitro characteristic properties of the nanoparticles were evaluated by particle size and zeta potential, DSC, XRD, FT-IR and 1H-NMR analyses. MET amount was evaluated by a modified HPLC method.

RESULTS:

Compositions of the MET incorporated polymeric nanoparticle formulations were presented in Table 1.

Table 1. Compositions of the formulations prepared

Code	KSR (mg)	MET (mg)	T80 (0.5 % w/v) (mL)
F0	250	-	25
F1	250	10	25
F2	250	25	25
F3	250	50	25
F4	250	75	25

The in vitro characterization analyses results revealed that the MET incorporated nanoparticles were formulated emulsification-solvent evaporation method and dry particles were collected after being lyophilized. Particle size analyses revealed that the particles were within the nanometer range with relatively high polydispersity index data. DSC and 1H-NMR analyses revealed the physical incorporation of MET into the polymeric nanoparticles.

CONCLUSIONS:

Incorporation of MET into the polymeric nanoparticles were achieved successfully and the in situ gelling formulations will be formulated for vaginal application of MET.

ACKNOWLEDGEMENTS:

DOPNA-LAB (FT-IR and 1H-NMR), Faculty of Science (XRD)

REFERENCES:

1. Mbah C, Builders P et al., (2014). Journal of Drug Delivery Science and Technology 24 (6) 565-571.
2. Castelli F et. al., (2003). Thermochimica Acta 400, 227.

P-316: PREPARATION OF HEPARIN-LOADED NANOFIBERS USING TWO DIFFERENT CORE SOLUTIONS

Ruzgar Ozemre, G., Tort, S., Acarturk, F.

Gazi University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Etiler Ankara Turkey

INTRODUCTION:

Low-molecular-weight heparins(LMWH) are negatively charged, water soluble, highly sulfated oligosaccharide fragments derived from commercial grade heparin by controlled depolymerization. Heparin and its derivatives are only used parenterally. Administration of oral heparin is thought to be a good alternative to parenteral heparin and other anticoagulant drugs1 .

The aim of this study was to prepare coaxial LMWH nanofiber for oral delivery by using co-axial electrospinning method with two different core solutions.

MATERIALS AND METHODS:

Materials: LMWH (Enoxaparin Sodium), Eudragit® S100 and Polyox® WSRN10(PEO) was kindly donated by Atabay Chemicals (Turkey),Evonik (Germany) and Dow Chemicals(Germany) respectively. Ethanol, toluidin blue, hexane, propylene glycol(PG), dimethylformamide was purchased from Sigma (Germany). All other chemicals and reagents were of analytical grade.

Properties of Shell and Core Solutions:The nanofibers prepared in the core-shell structure by coaxial electrospinning. The purpose of preparing two different core solutions was to prevent clogging of the nozzle with polymer solution.Two different core solutions were prepared. One of them core was obtained by adding of 500 mg LMWH and 250mg

PEO into 5 mL distilled water; the other was consist of 500mg LMWH, 2.5mL propylene glycol and 2.5 mL distilled water. Shell solution was obtained by solving of 1,5gr Eudragit S100 in 6mL ethanol:4mL dimethyformamide mixture.

Electrospinning Process: Electrospinning process was conducted using NE-300 Laboratory Scale Electrospinning Unit. The distance between coaxial needle and collector was 12cm. Applied voltage was set to 14kV. The flow rates of core and shell solutions were set 0,5ml/h and 1ml/h, respectively.

The Amounf of Loaded Heparin: Drug content of LMWH in nanofibers was assayed in pH 7,4 buffer with spectrophotometric measurement method based on methachromatic assay with toluidine blue.

RESULTS:

Viscosity, conductivity and the surface tension values of the polymer solutions used in the electrospinning process are the most criticial parameters for production2.The properties of the shell and core solutions are shown on following table.

	Shell solution	Core solution (with PEO)	Core solution (with PG)
Viscosity(Brookfield, DV-III Rheometer, USA) mPa.s	63	14	2
Conductivity(Hanna Instruments, HI 9033,1 USA) µS/cm	65,7	1294	295
Surface tension(Attension-Theta Lite, Biolin Scientific Finland) mN/m	24,20	13,73	83,27

Co-axial electrospinning process was successfully performed with these parameters. The amount of encapsulated heparin loaded to nanofiber containing PEO was found to be more than that of the fiber containing PG.

CONCLUSIONS:

LMWH was succesfully loaded in to the nanofibers by adding of PEO to the core solution. Co-axial nanofibers prepared with Eudragit and PEO may be a promising delivery system for oral administration of LMWH.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-117S206)

REFERENCES:

1. Neves, A. R., Correia-da-Silva, M., Sousa, E., & Pinto, M. (2016). Strategies to Overcome Heparins' Low Oral Bioavailability. Pharmaceuticals, 9(3), 37.
2. Frenot, A., & Chronakis, I. S. (2003). Polymer nanofibers assembled by electrospinning. Current opinion in colloid & interface science, 8(1), 64-75.

P-317: SOLID LIPID NANOPARTICLES FOR ORAL ADMINISTRATION: HIGH PRESSURE HOMOGENIZATION METHOD

Erkan, O., Amasya, G., Sezgin-Bayındır, Z., Yuksel, N.

Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Solid lipid nanoparticles (SLNs) which combine the features of liposomes, nanoemulsions and polymeric nanoparticles are rapidly developing field of nano drug delivery systems. SLNs prepared by physiological and biodegradable lipids can be administered via various routes such as parenteral, oral, dermal and transdermal. The advantage of orally administrated SLNs is the enhancement of oral absorption/ bioavailability of the drug molecules and providing sustained drug release (1). Hot homogenization which is carried out at temperatures above the melting point of lipids does not require organic solvent usage. Initially, a pre-emulsion of the melted lipid - aqueous emulsifier phase should be prepared by a high-shear mixing device like ultraturrax, and then the size of the droplets must be reduced to nanoscale via ultrasonication or high pressure homogenization (2).

The main goal of this study is to prepare SLNs with suitable particle size, polydispersity index and zeta potential for oral absorption. For this purpose High Pressure Homogenization (HPH) and ultrasonication methods were compared for the nanonization of the pre-emulsion and obtaining stable SLNs.

MATERIALS AND METHODS:

In this study two different techniques namely ultrasound and high pressure homogenization were used to reduce droplet size of hot pre-emulsions and as a process parameter different number of cycles were applied in HPH. Compritol 888ATO and Tristearin were selected as solid lipids and SLNs were stabilized by Ploxamer 188. The full characterizations of SLNs were exhibited by measuring the particle size, PDI and zeta potentials. The most suitable SLN formulation for oral drug administration was estimated.

RESULTS:

The results revealed that, it is possible to obtain lipid nanoparticles by combining high shear homogenization and HPH when tristearin was used as solid lipid at different concentrations. The particle sizes were in the nanometer range for all prepared SLN formulations with Tristearin and it was observed that both the particle size and the PDI values were decreased with the number of homogenization cycle.

CONCLUSIONS:

The findings showed that HPH which is combined with high shear homogenization seem to be an appropriate

method for SLN production. On the other hand, lipid type was found to be important for obtaining stable SLNs. The obtained SLN formulations demonstrate suitable physicochemical properties for oral drug administration and further studies will be conducted to develop drug loaded SLNs for this purpose.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-115S339)

REFERENCES:

1. Mehnert W., Mader K. (2001). Advanced Drug Delivery Reviews. 47, 165-196.
2. Wissing et. al, (2004). Advanced Drug Delivery Reviews. 56: 1257-1272.

P-318: FORMULATION AND EVALUATION OF SPRAY DRIED CHITOSAN NANOPARTICLES OF LEVOCETIRIZINE DIHYDROCHLORIDE FOR ANTIHISTAMINIC TREATMENT

Yurtdas Kirimoglu, G., Özturk, AA.,

[1] Anadolu University, Department of Pharmaceutical Technology, Eskisehir, Turkey

INTRODUCTION:

Levocetirizine dihydrochloride (LCD) is a third generation non-sedative antihistamine. LCD works by blocking histamine receptors. It does not prevent the actual release of histamine from mast cells, but prevents it binding to receptors. In addition, it is an important drug in the treatment of allergies and idiopathic urticaria (1). Chitosan (CS) is a natural biodegradable and biocompatible polysaccharide (2). In this study; LCD loaded CS nanoparticles prepared by spray-drying method for extended antihistaminic delivery of oral use was aimed in this study.

MATERIALS AND METHODS:

LCD is kind gift from Neutec Pharma (Sakarya/ Turkey). CS (LMW) purchased from Sigma, Germany. Spray drying technology (B-190, BUCHI) was used for the preparation of nanoparticles with an inlet temperature of 120°C ± 1°C and outlet temperature 60 °C ± 5 °C. Compositions of formulations prepared are summarized in Table 1. During the characterization studies particle size, polydispersity index, morphology, zeta potential and thermal analyses were performed.

Table 1. Compositions of formulations prepared

Code	Chitosan (g)	LCD (g)	Acetic acid solution (2%, v/v) (mL)	Methanol (mL)
Placebo	1	-	120	120
F-1	1	0.05	120	120
F-2	1	0.1	120	120

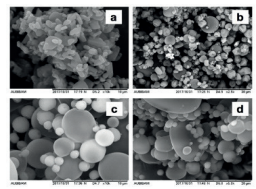
RESULTS:

Particle size, zeta potential measurements (Table 2), morphological analyses (Figure 1) were shown for the characterization of the systems prepared.

Table 2. Mean particle size, PI, zeta potential of formulations prepared (SE: Standard Error) (n=3)

Code	Particle size (nm) ± SE	PI ± SE	Zeta Potential (mV) ± SE
Placebo	487.42 ± 7.25	0.426 ± 0.085	24.3 ± 2.1
F-1	521.70 ± 8.50	0.512 ± 0.090	25.7 ± 1.8
F-2	538.46 ± 5.74	0.498 ± 0.074	25.9 ± 2.5

Figure 1. SEM Images of pure drug and formulations prepared (a: LCD, b: Placebo, c: F-1, d: F-2)



CONCLUSIONS:

LCD could be incorporated successfully into polymeric nanoparticles. Smaller particle size, cationic zeta potential indicated by characterization methods, possible LCD polymeric matrix interaction were determined to be a promising approach for extended delivery of LCD.

REFERENCES:

1. Vino S et al. (2012). Journal of Applied Pharmaceutical Science 02(08):221-225
2. Thapa B, Narain R (2016). In:Narain R (ed.) Polymers and Nanomaterials for Gene Therapy. Woodhead Publishing is an imprint of Elsevier, London, UK. pp 1-27

P-319: NOVEL STRATEGIES TO SYNTHSESIS OF POLYMER-DRUG CONJUGATE BY CHARGE TRANSFER COMPLEX COPOLYMERIZATION

Kaplan Can, H., Parvizi Khosroshahi, S.

Hacettepe University, Faculty of Science, Department of Chemistry, Ankara, Turkey

INTRODUCTION:

Interdisciplinary research at the interface of polymer chemistry and the biomedical sciences has produced polymer-based nanomedicines for the diagnosis and treatment of cancer. Water-soluble hybrid materials as polymer-drug conjugates are designed for intravenous administration. 5- Fluorouracil (5-FU) with the wide range of usage and is one way the need as well as a single agent administered to the patient

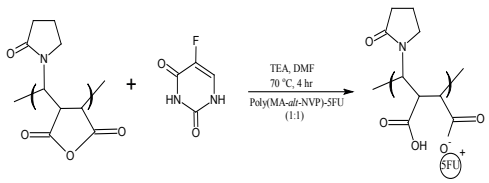
intravenously in combination with anticancer drugs. It is possible to increase the activity of 5-FU and eliminate/or minimize side effects with polymer/5-FU conjugation in biological systems (1).

MATERIALS AND METHODS:

Synthesis of copolymer and copolymer/5-FU are characterized and enlightened the conjugation mechanism by Fourier Transform Infrared (FTIR) and Nuclear Magnetic Resonance (1H, 13C NMR), X-ray Diffraction (XRD) and HR-Raman spectroscopic methods (Scheme 1). Biological activity of copolymer and its 5FU conjugate were investigated via Saos-2 cells by using the dsDNA method to assess the number of viable cells and cell proliferation.

RESULTS:

Obtained poly(maleic anhydride-alt-vinyl pyrrolidone) poly(MA-alt-NVP) and poly(MA-alt-NVP)-5FU via charge transfer complex (CTC) copolymerization properties were clarified by using FTIR, NMR (1H, 13C), XRD and HR-Raman spectroscopic methods by following characteristic bands and their locations (1).



Scheme 1. Conjugation of of Poly(MA-alt-NVP) with 5-FU

CONCLUSIONS:

The results confirmed that copolymerization of MA:NVP system formed CTC and reaction preceded via alternating copolymerization mechanism. Obtained results from the dsDNA method, copolymer shows higher cell viability against Saos-2 cells than the copolymer-drug conjugate.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (KBAG-114Z682).

REFERENCES

1. ParviziKhosroshahi S, Kaplan Can H (2018). Journal of Macromolecular Science, Part A: Pure and Applied Chemistry, 55:192-204.

P-320: DETERMINATION OF IN-VITRO SIMILARITY BY AERODYNAMIC PARTICLE SIZE DISTRIBUTION BETWEEN TEST PRODUCT AND REFERENCE PRODUCT IN NEBULISATION FORM INCLUDING SABA / ANTICHOLINERGIC COMBINATION

Icin H., Turk M., Keskin G., Isik E., Tanriver K., Gokalp M., Dude U.

Abdi İbrahim Pharmaceuticals, Research and Development Center, Istanbul, Turkey

INTRODUCTION:

Establishing relationships between in vitro and in vivo data for Drug Products is an important goal of development process. For pulmonary Drug Product an in vitro characterized aerodynamic particle size distributions (APSDs) are expected to have some predictive power not only for drug deposition in various area of lungs, but also for clinical effects. In this study, in-vitro profiles of the test product and the reference product were compared in the form of nebulization containing selective beta-2-adrenoceptor agonist and anticholinergic, used in the treatment of reversible bronchospasm associated with obstructive airway diseases, in patients in need of more than one bronchodilator.

MATERIALS AND METHODS:

In-vitro profiles were obtained by Aerodynamic Particle Size Distribution analysis using Next Generation Impactor (NGI) (1). The conditions set out in the European Medicines Agency's (EMA) guidelines (2,3) were considering during the study. Justified groups of impactor stages were generated in order to provide in-vitro profiles. Justification was based on the expected deposition sites in the lungs. Three batches of the test product and three batches of the reference product were tested during the study. The % difference between mean values of test product and reference product and 90% confidence intervals for the differences were calculated for each group.

RESULTS:

The in-vitro profile similarity of the test product and the reference product has been proved by checking the conformity of difference to +/- 15% acceptance criteria.

CONCLUSIONS:

According to EMA Guideline, establishment of such degree of similarity between Reference and Generic Product is evidence for expected equivalence in terms of both safety and efficacy of pharmaceutical products.

REFERENCES:

1. European Pharmacopeia (Ph. Eur.) 2.9.18. Preparations for Inhalation: Aerodynamic Assessment of Fine Particles.

2. EMA - Guideline on The Requirements For Clinical Documentation For Orally Inhaled Products (OIP) Including The Requirements For Demonstration of Therapeutic Equivalence Between Two Inhaled Products For Use In The Treatment of Asthma And Chronic Obstructive Pulmonary Disease (COPD) In Adults And For Use In The Treatment of Asthma In Children And Adolescents (Doc. Ref: CPMP/EWP/4151/00 Rev.1).
3. EMA - Guideline on The Pharmaceutical Qualıty of Inhalation And Nasal Products (Doc Ref: EMEA/CHMP/QWP/49313/2005 Corr).

P-321: 3D PRINTING AS A NEW TOOL FOR THE DEVELOPMENT OF SOLID DOSAGE FORMS

Gultekin, HE., Tort, S., Acarturk, F.

Gazi University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Etiler Ankara Turkey

INTRODUCTION:

3D printing (3DP) is a layer-by-layer manufacturing process which is used to prepare a 3D object utilizing computer aided design data.1 Fused deposition modeling (FDM) is a recently used 3DP technology.2 Pramipexole is a widely used drug which treats the symptoms of Parkinson's disease.3 It was chosen as a model drug for the personalized treatment purpose of the 3D printing.

The aims of the present study were to prepare 3D printed pramipexole tablets, to determine the pharmaceutical properties of the obtained tablets and to evaluate the 3D printability of a hot melt extrudable form of hypromellose.

MATERIALS AND METHODS:

Pramipexole dihydrochloride monohydrate, polyethylene oxide N80 (PEO N80) and AffinisolTM were kindly donated from Deva Pharmaceuticals and Dow Chemical Company, respectively. A hot melt extrusion (HME) method was carried out using Filabot Filament Extruder in order to fabricate drug loaded filaments. By using the obtained filaments 3D printed tablets were fabricated via MakerBot® Replicator_ 2X Experimental 3D Printer. The physico-pharmaceutical properties of the 3DP tablets were measured and the amount of drug in the tablets and filaments were determined. Also in vitro dissolution study for the 3DP tablets was performed.

RESULTS:

The physico-pharmaceutical properties of the 3DP tablets are shown in Table 1 and the in vitro drug release profile of the 3DP tablets is shown in Figure 1.

Table 1. The physico-pharmaceutical properties of the 3DP tablets.

Weight Uniformity (mg)	Dimensions	
	Diameter (mm)	Thickness (mm)
150±8	2,09±0,08	9,93±0,12

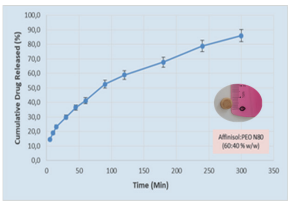


Figure 1. The in vitro drug release profile of 3DP tablets.

The physico-pharmaceutical properties showed that the 3DP tablets have good reproducibility and the in vitro drug release profile of the tablets demonstrated that more than 85% of the drug was relesed from the tablets within 5 hours.

CONCLUSION:

Drug loaded filaments were successfully fabricated by HME and the tablets were successfully printed by FDM. This study demonstrates that FDM-3D printing is an effective technology for the development of solid dosage forms. AffinisolTM, as a hot melt extrudable form of hypromellose, is a suitable polymer for FDM. By combining different polymers with AffinisolTM, the drug release profile of the 3DP tablets can be optimized.

REFERENCES:

1. Norman, J.; Madurawe, R. D.; Moore, C. M.; Khan, M. A. and Khairuzzaman, Adv. Drug Del. Rev., 108, 39-50 (2017).
2. Goyanes, A.; Chang, H.; Sedough, D.; Hatton, G. B.; Wang, J.; Buanz, A.; Gaisford, S. and Basit, A. W. Inter. J. Pharm., 496(2), 414-420 (2015).
3. Putri, R. S.; Setiawati, E.; Aziswan, S. A.; Ong, F.; Tjandrawinata, R. R. and Susanto, L. W. Sci. Pharm., 84(4), 715-723 (2016).

P-322: PREFORMULATION STUDIES OF NANOPARTICLES FOR PSORIASIS DISEASE TREATMENT

[1] Erol, I., [2] Ustundag Okur, N., [1] Ozer, O.

[1]Ege University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Izmir, Turkey

[2]Istanbul Medipol University, School of Pharmacy, Department of Pharmaceutical Technology, Istanbul, Turkey

INTRODUCTION:

Psoriasis is one of the most common human skin diseases and is considered to have key genetic underpinnings. It is characterized by excessive growth and aberrant differentiation of keratinocytes (1). The aim of the study is to develop topical nanocarriers of tazarotene to treat psoriasis disease with minimal side effects and maximum efficiency.

MATERIALS AND METHODS:

Solid lipid nanoparticles (SLNs) were prepared by high shear homogenization method at 24000 rpm (2). Suppocire was chosen as solid lipid, Poloxamer 188 as surfactant and bidistilled water as water phase. Preformulation studies carried out using several amounts of Suppocire (100, 200 and 300 mg) and Poloxamer 188 in order to prepare the most desirable carrier. Finally, 100 mg of Suppocire were chosen for SLN formulation. The unloaded SLN formulations were characterized by means of their particle size and polydispersity index (PDI). The average particle size and PDI measurement were performed via dynamic light scattering method using Malvern Zetasizer (Nano ZS, Malvern Instruments, U.K.) at an angle of 173° at 25 °C.

RESULTS:

The SLN carriers were successfully developed using 100 mg Suppocire in 25 ml of water (Table 1). Particle size of SLNs ranged from 204-1146 nm. As it can be seen from Table 1, better PDI (<0.5) could be observed using higher poloxamer amount (F3, F4, F5 and F6). Therefore F3 formulation (100 mg Suppocire and 350 mg poloxamer in 25 ml of water) was selected as the optimized formulation which can be used against psoriasis.

Table1. Compositions, particle size and PDI measurements of different SLN formulations

Formulation code	Suppocire (mg)	Poloxamer188 (mg)	Water (ml)	Particle size (nm)	PDI
F1	100	15	25	1446±240.30	0.780±0.070
F2	100	25	25	1389±449	0.766±0.207
F3	100	350	25	204.9 15.49	0.311±0.116
F4	100	400	25	364±13.46	0.405±0.029
F5	100	450	25	315±13.17	0.451±0.115
F6	100	500	25	292±50.16	0.468±0.030

CONCLUSIONS:

SLNs prepared by high shear homogenization method could be offered as a promising strategy for topical drug delivery.

ACKNOWLEDGEMENTS:

This study was supported by University of Ege, Faculty of Pharmacy and Department of Pharmaceutical Technology (16/ECZ/010).

REFERENCES:

1. Lowes MA, Bowcock AM, Krueger JG (2007). Pathogenesis and therapy of psoriasis., 445:866–873.

P-323: PREPARATION, CHARACTERIZATION AND CELL VIABILITY STUDIES OF CISPLATIN LOADED SELF-MICROEMUSIFYING DRUG DELIVERY SYSTEM (SMEDDS)

[1] Akartas, I., [2] Karasulu, HY.

[1]European University of Lefke, Faculty of Pharmacy, Lefke, Turkish Republic of Northern Cyprus

[2]Ege University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Izmir, Turkey

INTRODUCTION:

Cisplatin is an antineoplastic drug, used for the treatment of ovarian cancer. SMEDDS has many advantages such as enhanced bioavailability, lymphatic absorption and ease of manufacture (1,2). The aim of this study was to prepare and characterize Cisplatin loaded SMEDDS formulation and to evaluate in vitro release studies and antitumoral activity with cell viability studies.

MATERIALS AND METHODS:

Firstly, pseudoternary phase diagrams were constructed using water titration method in order to determine the stable microemulsion range. The physicochemical properties of microemulsions such as physical appearance, pH, refractive index, viscosity, droplet size, polydispersity index (PDI), zeta potential, distribution stability was measured in order to evaluate characteristic properties of microemulsion. In vitro release studies of Cisplatin loaded SMEDDS were performed with dialysis membrane. Samples were analysed considering the calibration curve with HPLC method (Shimadzu, Japan) which is validated. The effect of Cisplatin SMEDDS formulation was determined by MTT assay on A2780 cell line. A2780 cell line is a human ovarian carcinomic cell line which is procured by European Collection of Cell Cultures (ECACC). Cell viability was evaluated with ELISA microplate reader-UV spectrophotometer (Thermo vario scan-FHA multiplate reader) at 570 nm

RESULTS:

Cisplatin SMEDDS were measured as 25,4±1,9 nm and PDI was 0,241±0,018. Refractive index of the formulation measured as 1,471±0,001. pH value of Cisplatin SMEDDS diluted by water with the dilution ratio 1:10 was measured as 5,84±0,09 and Cisplatin SMEDDS diluted by pH 6,8 PBS with the dilution ratio 1:10 was measured 6,51±0,14. Viscosity of formulation was measured as 284 mPa and in vitro release studies were performed and 78,17% of cisplatin was released. The formulation performed cytotoxic effect to A2780 cells with 20,26% vitality at 0,02 µg/mL.

CONCLUSIONS:

It was concluded that, Cisplatin SMEDDS is an advantageous formulation for the treatment of ovarian cancer with its antitumoral activity. This formulation could be a promising alternative due to its less side effects and enhanced lymphatic absorption.

REFERENCES:

1. Kalepu S et al., (2013). Acta Pharmaceutica Sinica B, 3(6):361-372.
2. Vasconcelos T et al., (2018). European Journal of Pharmaceutics and Biopharmaceutics, 123:1-8.

P-324: TRANSDERMAL DELIVERY OF AN ANTIEPILEPTIC DRUG: LACOSAMIDE

[1] Aykac, K., [2] Basaran, E.

[1] Anadolu University, Institute of Health Sciences, Eskişehir, Turkey

[2] Anadolu University, Department of Pharmaceutical Technology, Eskişehir, Turkey

INTRODUCTION:

Among the antiepileptic agents, Lacosamide (LAC); a third-generation antiepileptic-drug has a novel mechanism of action (1). In our study considering the frequent incidance of epilepsy in infants and elderly people, preliminary formulation studies of transdermal delivery systems for Lacosamide, which will be very confortable in use for the proposed aged groups, were conducted.

MATERIALS AND METHODS:

Lacosamide and Kollidon® SR (KSR) were gifted kindly from Santa Farma (İstanbul, Turkey) and BASF (İstanbul, Turkey) respectively. Chitosan was purchased from Fluka Chemicals (Steinheim, Germany). Eudragit® RS 100 (ERS 100) was purchased from Röhm Pharma Polymers (Darmstadt, Germany). Tween® 80 (T80) was obtained from Merck (Hohenbrunn, Germany). All other chemicals were in analytical grade.

Nanoparticles were prepared by emulsification-solvent evaporation method (2). In vitro characteristic properties of the nanoparticles were evaluated. Lacosamide amount was evaluated by a modified HPLC method. Due to the unique cationic character, gel and film forming properties transdermal formulation were prepared with chitosan.

RESULTS:

Formulations were prepared by different amounts of Lacosamide in order to achieve highest incorporation efficiency (Table 1).

Table 1. Compositions of the formulations prepared (*DCM: Dichloromethane, ACE: Acetone)

Code	KSR (mg)	ERS 100 (mg)	LAC (mg)	T80 (1% w/v) (mL)	DCM (mL)	ACE (mL)
F0	100	100	-	4	1	1
F1	100	100	20	4	1	1
F2	100	100	50	4	1	1
F3	100	100	100	4	1	1

The in vitro characteristic properties of the particles were evaluated by particle size and zeta potential, DSC, XRD, FT-IR and 1H-NMR analyses. The analyses results revealed that the particles were in amorphous state and Lacosamide was molecularly dispersed within the polymeric structure.

CONCLUSIONS:

As the preliminary study, the in vitro characteristic properties of the nanoparticles were evaluated in detail and analyses results revealed that Lacosamide incorporated polymeric nanoparticles were prepared successfully by emulsification-solvent evaporation method.

ACKNOWLEDGEMENTS:

DOPNA-LAB (FT-IR and 1H-NMR), Faculty of Science (XRD)

REFERENCES:

1. Liguori C, Izzi F et al. (2018). Epilepsy & Behavior Case Reports doi:10.1016/j.ebcr.2018.02.004
2. Crucho CIC, Barros MT (2017). Materials Science and Engineering C, 80:771-784.

P-325: PREPARATION AND CHARACTERIZATION OF QUERCETIN LOADED CYCLODEXTRIN/CHITOSAN/TPP NANOPARTICLES

[1] Guven, UM., [2] Gulec, K., [3] Berkman, MS., [3] Demirel, M.

[1] Cukurova University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Adana, Turkey

[2] Anadolu University, Graduate School of Health Sciences, Department of Biochemistry, Eskisehir, Turkey

[3] Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Eskisehir, Turkey

INTRODUCTION:

Quercetin (Qu) is a polyphenolic flavonoid that has been shown to have anti-inflammation, anti-viral, anti-allergic, anti-oxidant and anti-cancer activities (1). Its use in pharmaceutical field is limited by its low aqueous solubility. Cyclodextrin/chitosan/pentasodium tripolyphosphate nanoparticles (CD/CS/TPP-NPs) has been developed as a new carrier for poorly water-soluble drugs. The aim of this study was to prepare, characterize the Qu loaded CD/CS/TPP-NPs and evaluate their potential for the anti-oxidant activity.

MATERIALS AND METHODS:

The Qu-CD/CS/TPP-NPs were prepared with Qu-methyl beta-CD inclusion complex and MMW CS. Ionotropic gelation technique was used for the preparation of NPs (2). The characteristics of NPs were evaluated by particle size, DSC, XRD, NMR, FT-IR, SEM, encapsulation efficacy, in vitro release and anti-oxidant activity studies. In vitro release studies were carried out for 24h with PBS at pH6.8 in a dialysis tube (MWCO:14,000Da) (n=3). Anti-oxidant activity studies on NPs were carried out with DPPH test (n=6).

RESULTS:

The prepared NPs were formed with controlled size of 202.3-335.6nm and a PDI ranged from 0.449 to 0.585 with good encapsulation efficiency of up to 67.71%. FT-IR, DSC and NMR studies revealed that CD and Qu were effectively integrated into the NPs. NPs showed a higher release than pure Qu and lower release than Qu-CD. DPPH test results showed that NPs exhibited high anti-oxidant activity up to 99.00% (Table 1).

Table 1. Anti-oxidant activity of plasebo (PL), Qu, Qu-CD and NPs (n=6, mean±SD)

Conc. (µg/mL)	Antioxidant Activity (%)								
	PL	Qu	Qu-CD	F2-1	F2-3	F3-1	F3-3	F4-1	F4-3
1	2.5±0.3	55.9±0.2	57.4±0.5	76.0±0.3	74.9±0.2	75.4±0.1	63.0±0.4	63.3±0.2	62.0±0.2
5	3.4±1.3	74.7±0.1	81.1±0.5	99.0±0.9	94.2±0.2	93.9±0.1	88.6±0.3	83.9±0.2	86.0±0.3

CONCLUSIONS:

In vitro release of Qu from the NPs showed controlled release compared to the Qu-CD alone, but the moderate release rate of Qu-CD/CS/TPP-NPs could be better to sustain the time of drug action. Additionally, the increased anti-oxidant activities of Qu were correlated with improvement in physicochemical characterization.

ACKNOWLEDGEMENTS:

This study was financed by Anadolu University Scientific Research Project Foundation (No.1502S059)

REFERENCES:

1. Liu et al. (2017). Biomedicine&Pharmacotherapy, 92:33-38.
2. Trapani et al. (2010). European Journal of Pharmaceutics and Biopharmaceutics, 75:26-32.

P-326: PHYSICOCHEMICAL STABILITY AND COMPATIBILITY TESTING OF METRONIDAZOLE IN PARENTERAL NUTRITION MIXTURES

Dettlaff K., Popielarz Brzezińska M., Gostyńska A.

Poznan University of Medical Sciences, Department of Pharmaceutycal Chemistry, Poznań, Poland

INTRODUCTION:

Co-administration of parenteral nutrition (PN) with medicines without proven compatibility and stability tests is considered as a medical error. Addition of the drug to the PN can lead to incompatibilities of the components of the mixture with the drug, decrease in the stability of o/w emulsions and catalyze of the drug degradation [1]. However, coadministration of the drugs in one bag with a PN mixture could reduce the risk of vascular access complications and infections, as well as protect against overhydration of the patient.

The aim of this study was to determine the possibility of addition of metronidazol to selected PN mixtures before administration to the patient.

MATERIALS AND METHODS:

PN mixtures (6 compositions) with the tested drug at a daily dose of 1500 mg, as well as analogous mixtures without drug were stored for 7 days at 5±1 ºC, then

for another 24 hours at 23±1 ºC with light exposure (conditions of PN administration to the patient). The pH of the mixtures, the color (CIEL*a*b* system), the size of the lipid emulsion particles and the zeta potential was determined every 24 hours. The metronidazole content was determined using HPLC method.

RESULTS:

During the 8 days of the study, no macroscopic signs of emulsion degradation were observed and the color of PN mixtures was unchanged ($\Delta E<1$). The pH of the mixtures was in the range 6.19-6.38 depending on the composition of the mixture and did not change during storage (maximum different ± 0.05). The lipid emulsion particle size was in the range 210-230 nm (pharmacopoeial limit < 500 mn) and the zeta potential varied form 22.0 mV to 8.3 mV. The maximum decrease in the content of metronidazole in studied PN mixtures after 8 days was 5%.

CONCLUSIONS:

Previous reports have shown the possibility of simultaneous administration of metronidazole via the Y-site together with some ready-to-use mixtures [2], in this study we showed that Metronidazole B.Braun 5 mg/ml can be added to 6 different mixtures and stored up to 7 days at 5 ºC before administration to the patient.

ACKNOWLEDGEMENTS:

This study was supported by grant SONATA no. 2015/17/D/NZ7/00792 from the National Science Centre, Poland.

REFERENCES:

1. Mühlebach S (2009). E Spen Eur E J Clin Nutr Metab 4:e134–e136.
2. Staven V, Iqbal H, Wang S, Grønlie, Tho I (2017). J Pharm Pharmacol 69:448-462.

P-327: IS COMBINING OF DRUGS WITH TPN MIXTURES SAFE? COMPATIBILITY STUDIES OF SOME FLUOROQUINOLONES WITH TPN

Gostyńska A., Stawny M., Dettlaff K., Jelińska A.

University of Medical Sciences, Department of Pharmaceutical Chemistry, Poznań, Poland

INTRODUCTION:

Pharmacotherapy of patients receiving total parenteral nutrition (TPN) is a common clinical problem due to the limitation of oral medications administration. This is very important especially for critically ill patients who, in extreme cases, receive even several intravenous infusions at the same time, which raises real technical problems with the method of their administration, due to the limited number of venous access. One of the solution is co-administration of drugs with TPN mixture via Y-site. However, this procedure have to be preceded by tests confirming compatibility of the drug with the TPN mixture. The aim of the study was to determine the compatibility of ciprofloxacin and levofloxacin with TPN mixtures when administrating via Y-site.

MATERIALS AND METHODS:

Twelve different compositions of TPN mixtures were mixed together with ciprofloxacin and levofloxacin in the ratio 1:1, 2:1 and 1:1, 1:2, respectively. The ratio was calculated based on infusion rates of both medications and TPN mixtures. The compatibility of the drugs with studied TPN mixtures was evaluated by visual and microscopic assessment, the pH, the osmolality, the lipid emulsion particles size (Dynamic Light Scattering method), and the zeta potential (Laser Doppler-Electrophoresis method). Each parameter was determined just after mixing (t=0), after 4 and 24 hours.

RESULTS:

Obtained results differed completely depending on the tested drug. In all samples with ciprofloxacin precipitation process occurred after 4 or 24 hours of storage, what was confirmed by microscopic assessment. On the other hand samples with levofloxacin show no macroscopic signs of precipitation nor emulsion degradation. The lipid emulsion particle size after addition of levofloxacin to TPN mixtures, within first 24 hour, was in the range 212.2 nm – 243.0 nm and meets the pharmacopoeial limit (< 500 nm). The zeta potential differ depending of TPN mixture composition and it was in the rage -13.3 mV to -4.8 mV. The pH of the mixtures was in the range 5.90 – 6.32 and 5.77 – 6.20 just after addition of the drugs and decreased by maximum 0.35 and 0.05 for ciprofloxacin and levofloxacin, respectively.

CONCLUSIONS:

The results of this study have shown that levofloxacin is compatible with TPN mixtures when administrating via Y-site in ratio 1:1 and 1:2. In contrary, it is impossible to co-administrated ciprofloxacin with TPN mixtures due to the drug precipitation.

ACKNOWLEDGEMENTS:

This study was supported by grant SONATA no. 2015/17/D/NZ7/00792 from the National Science Centre, Poland.

P-328: VALIDATION OF AN HPLC METHOD FOR THE DETERMINATION OF BESIFLOXACIN HCL FROM OCULAR INSERT BASED ON POLYCAPROLACTONE

[1] Polat, K., [1] Bozdag Pehlivan S., [2] Kır, S.,[1] Calıs S.,

[1] Hacettepe University, Faculty of Pharmacy, Dept. of Pharmaceutical Technology, Ankara, Turkey

[2] Hacettepe University, Faculty of Pharmacy, Dept. of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Besifloxacin, a broad spectrum antibiotic of the fourth generation fluoroquinolone group, has been reported to be effective in the treatment of bacterial keratitis (1). Validation is an important issue in pharmaceutical analysis and widely required in formulation development. In this study, it is aimed to develop and validate an HPLC method for the determination of Besifloxacin HCl (BH) from polycaprolactone (PCL) insert for the treatment of bacterial keratitis.

MATERIALS AND METHODS:

The selective assay of BH was carried out by HPLC according the to the modified method of Rajput et al. (2). HPLC system consisted of Agilent 1100 Separations Module equipped with ultraviolet (UV) detector (297 nm) and a C8 column (250 nm x 4,6 mm x 5 µm). The mobile phase was phosphate buffer adjusted pH 3 with ortophosphoricacid: methanol: acetonitrile in the ratio of 50:25:25 at flow rate of 1mL/min. In order to determine the amount of BH in PCL inserts, the drug loaded inserts were dissolved in 2 mL of dichlorometane:dimethylformamide:methanol mixture. The samples were then put on an ultrasonic bath for 30 minutes and 1 mL PBS was added. Then, final mixture was centrifuged at 14000 rpm for 10 minutes. The supernatants were separated and filtered through 0.45 µm membrane filters and then injected to the HPLC column. The amount of BH in inserts was calculated through the peak area values by the calibration curve.

RESULTS:

The retention time was about 5.5 min. Calibration curve was linear over the concentration range of 0,03-1 µg.mL-1 . The intra- and inter-day precision relative standard deviation was 2.03 % or less, and the accuracy was within 0.78 % of the nominal concentration.

CONCLUSIONS:

The developed HPLC method was succesfully applied to quantitate BH in ocular insert based on PCL.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-217S126).

REFERENCES:

1. Stapleton F, Edwards K, Keay L et al., Ophthalmology, 119(8), 1516–1521, 2012.
2. Rajput S, Pandya C, Chaundhari P, Int. J. Chem. Pharm. Anal., 3(2),1-7, 2016.

P-329: BIOFUNCTIONALIZATION OF GRAPHENE OXIDE FOR DRUG DELIVERY APPLICATIONS

Demirhan, K.,Caliskan Salihi, E.

Marmara University, Faculty of Pharmacy, Department of Basic Pharmaceutical Sciences, Istanbul, Turkey

INTRODUCTION:

Graphene is a basic building block for carbon materials with different geometries and unique physical and chemical properties. Graphite oxide is an oxygen-containing and water-dispersible derivative of graphite, it can be exfoliated and well suspended in an aqueous medium even down to the single-layer level form of graphene oxide (1). Graphene-based materials have attracted strong interest in the recent studies in order to produce functionalized biosystems. Furthermore modification with biomolecules is advantageous because it improves the biocompatibility of the materials. In this context, biofunctionalization of graphene oxide using fatty acids was investigated in this study for drug delivery applications (2).

MATERIALS AND METHODS:

Graphene oxide was produced using Hummers method revised in our laboratory (1). Biofunctionalization was thereafter conducted by the addition of undecylenic acid followed by a heat treatment using a green route.

RESULTS:

Biofunctionalization experiments were conducted under several experimental conditions (i.e. temperature, treatment time etc.) in order to set up optimum conditions. Functionalization was followed by UV-Visible spectrophotometry. Then the samples were characterized by using XRD, FTIR and electron microscopy. Results of the characterization studies showed the successful functionalization of graphene oxide sheets.

CONCLUSIONS:

A new graphene based biofunctionalized material was produced in this study for drug delivery applications using green chemistry approach.

REFERENCES:

1. Caliskan Salihi E, Wang J, Coleman DJ, Šiller L (2016). Separation science and technology, 51(8):1317-1327.
2. Wang Y et al., (2011). Trends in Biotechnology, 29(5):205-212.

P-332: DEVELOPMENT AND CHARACTERIZATION OF SELF NANOEMULSIFIYING FORMULATION FOR ORAL PEPTIDE DELIVERY

[1,2] Celik Tekeli, M.,[2] Aktas, Y.,[1] Celebi, N.

[1]Gazi University Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

[2]Erciyes UniversityFaculty of Pharmacy, Department of Pharmaceutical Technology, Kayseri, Turkey

INTRODUCTION:

Self nanoemulsifiying drug delivery systems (SNEDDS) are isotropic mixtures of oils, surfactants, solvents and co-solvents/surfactants which form nanoemulsions with aqueous dilution in gastrointestinal tract by gentle agitation (1). The objective of this study was to develop a self nanoemulsifying formulation for oral peptide delivery.

MATERIALS AND METHODS:

In this study while preparing SEDDS; ethyl oleate was the oil phase whereas Cremophor EL® and Labrasol® were used as surfactant, absolute alcohol and propylene glycolwere used as co-surfactant. Pseudoternary phase diagrams were established by titration. The ratio of surfactant/co-surfactant (S/co-S) was selected as 3:1 from previous studies (2). The ratio of Cremophor EL® and Labrasol® was optimized using the following ratios: 1:1, 2:1, 3:1, 1:2, 1:3. Around the center of gravity, nanoemulsion existence field determined points of SEDDS were prepared. Prepared SEDDS were characterized for emulsification time, droplet size, polidispersity index and zeta potential at 40C storage conditions during one month. Statistical analysis were evaluated by one-way analysis of variance (ANOVA) test.

RESULTS:

The emulsification time of formulations are below one minute with bluish white appearance referred as Grade B formulations. The mean droplet size and polydispersity index of nanoemulsion containing 15% ethyl oleate in a ratio of Cremophor EL®/Labrasol® in different proportions were approximately 18-50 nm and 0.08-0.204 respectively. These formulations displayed no significant changes in both droplets size polydispersity index and emulsification times for one month ($p>0.05$).

CONCLUSIONS:

Five formulations containing 15% ethyl oleate as the oil phase, Cremophor EL®/ Labrasol® 2:1 and 3:1 as the surfactant mixture and propylene glycol as the co-surfactant were selected according to the characterization tests. These formulations will be evaluated for peptide encapsulation efficiency in further studies.

ACKNOWLEDGEMENTS:

This study was supported by Erciyes University Scientific Research Foundation (Project No: TCD-2017-7087).

REFERENCES:

1. Gursoy RN and Benita S. (2004). Biomedicine&Pharmacotherapy, 58:173-82.
2. Celik Tekeli M., Celebi N., Aktaş Y. (2017). Acta Pharmaceutica Hungarica, 87 (3-4): 112-112.

P-333: THE EFFECT OF CHITOSAN TYPE AND CONCENTRATION ON COMPLEXATION WITH SODIUM ALGINATE IN FILM FORMULATIONS

Ilhan, M., Kilicarslan, M.

Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Water-soluble sodium alginate is very popular natural polymer for many medical applications. Its anionic structure provides it cross-linking with cationic materials such as chitosan, a chemically active polymer because of its amino and hydroxyl groups. Carboxyl and amine groups of alginate and chitosan, respectively, can form polyelectrolyte complexes easily in suitable conditions (1-3). In this study clindamycin phosphate loaded alginate-chitosan adhesive polyelectrolyte complex films were prepared for periodontal drug delivery. The aim was to examine the effects of the chitosan type and concentration onto the formation of alginate-chitosan polyelectrolyte complex film.

MATERIALS AND METHODS:

Clindamycin phosphate loaded (1% (w/v)) polyelectrolyte complex films were prepared by solvent casting method (2,3) using alginate solution at 1%(w/v) concentration and chitosan (medium (F1-F3) and low (F4-F6) molecular weight) solutions at different concentrations (1% (F1, F4), 2% (F2, F5), 3% (F3, F6) (w/v)). CaCl2 (0.1%, w/v) and propylene glycol (5%, v/v) were used in all formulations. Thickness, viscosity, degree of swelling, adhesiveness of films, DSC analysis and in-vitro drug release studies were performed and evaluated for each film formulation.

RESULTS:

The viscosity of the mixture of polymer solutions before drying was significantly increased by the increase in concentration in both types of chitosan (from 0.23 ± 0.06 Pa.s (F4) to 5.63 ± 0.12 Pa.s (F3)). Polyelectrolyte complex formation was clearly showed by DSC thermograms. The highest swelling degree values were obtained with formulations prepared with 2% chitosan in both groups (F2 and F5). But the lowest peak force values obtained with formulations

prepared with 1% chitosan (F1 (1.101 ± 0.34 N) and F4 (1.317 ± 1.08 N)). These results showed that there was no correlation between swelling and adhesion due to non-homogenous complex formation. Drug release rate could be extended up to 6 hours with low molecular weight chitosan because of the higher complexation degree than that of medium molecular weight chitosan.

CONCLUSIONS:

The data obtained from present study clearly showed that solutions prepared with different molecular weight and concentrations of chitosan affected the film properties, significantly. Higher complexation was obtained with the formulations prepared using low molecular weight chitosan.

REFERENCES:

1. Unagolla JM, Jayasuriya AC (2018). Eur J Pharm Sci, 114, 199-209.
2. Kilicarslan M, Ilhan M (2018). 11th PBP World Meeting, Granada,Spain.
3. Kilicarslan M,Gorgoz M (2016). Drug Discovery 2016, Rome,Italy.

P-334: FORMULATION AND CHARACTERIZATION STUDIES OF ORNIDAZOLE INCORPORATED EUDRAGIT® S 100 BASED NANOPARTICLES

[1] Ali, MS., [2] Basaran, E.

[1]Anadolu University, Institute of Health Sciences, Eskisehir, Turkey

[2]Anadolu University, Department of Pharmaceutical Technology, Eskisehir, Turkey

INTRODUCTION:

Due to its excellent penetration, high tolerability, prolonged half-life and more favorable side-effects profiles than metronidazole, Ornidazole (ORN) is used for the treatment of many bacterial infection (1). In our study Eudragit® S 100 (ES-100) based polymeric nanoparticles were formulated and in vitro characteristic properties of the particles were evaluated.

MATERIALS:

ORN was kindly gifted by Abdi İbrahim İlaç (İstanbul, Turkey). ES-100 was purchased from Röhm Pharma Polymers (Darmstadt, Germany). Tween® 80 (T80) was obtained from Merck (Hohenbrunn, Germany). All other chemicals were in analytical grade.

METHODS:

Nanoparticles were prepared by emulsification-solvent evaporation method (2). A modified HPLC method was used for the determination of ORN. In vitro characteristic properties of the nanoparticles were evaluated in detail.

RESULTS:

Compositions of the formulations were presented in Table 1.

Table 1. Compositions of the formulations prepared

Code	ES-100 (mg)	ORN (mg)	T80 (0.5 % w/v) (mL)
M0	250	-	25
M1	250	10	25
M2	250	25	25
M3	250	50	25
M4	250	75	25

The in vitro characteristic properties of the particles were evaluated by particle size and zeta potential, DSC, XRD, FT-IR and 1H-NMR analyses. The analyses results revealed that the particles were in amorphous state and formulation stages did not influence the characteristic properties of the active agent.

CONCLUSIONS:

The in vitro characteristic properties of the nanoparticles were evaluated in detail and the analyses results showed that ORN incorporated polymeric nanoparticles were prepared successfully by emulsification-solvent evaporation method.

ACKNOWLEDGEMENTS:

DOPNA-LAB (FT-IR and 1H-NMR), Faculty of Science (XRD)

REFERENCES:

1. Zhang L et al., (2006). Journal of Pharmaceutical and Biomedical Analysis, 41: 1453-7.
2. Crucho CIC, Barros MT (2017). Materials Science and Engineering C, 80:771-784.

P-335: DRY GRANULATION: DETERMINATION OF OPTIMUM TABLETTING PARAMETERS USING COMPACTION SIMULATOR

Chunu, JT., Jiwa, N.,Ozalp Y.

Near East University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Lefkosa, TRNC

INTRODUCTION:

Compaction simulator is an equipment which is capable of mimicking the exact cycle of any tablet press in real time and using the data to define tabletting parameters. Dry granulation slugging process was used to improve the compactibility of paracetamol powder and formulations were designed to obtain optimum formulation and compressibility characteristics.

MATERIALS AND METHODS:

Table 1: Codes and composition of formulations.

Material	Supplier	DG-45-1 (%)	DG-45-2 (%)	DG-45-3 (%)	DG-45-4 (%)
Paracetamol	Kimetsan	45	45	45	45
Granulac® 70	Meggle	45	-	45	-
Flowlac® 100	Meggle	-	45	-	45
Stearic Acid	Kimetsan	2	2	2	2
Starch 1500®	Colorcon	4	4	8	8
Primogel®	FMC	2	2	-	-
Kollidon®PVPK90	BASF	2	2	-	-

The method used for obtaining paracetamol granules was slugging. The paracetamol powder was mixed with filler in a cubic mixer (Erweka) and 1% stearic acid was added as intragranular phase. Slugs were pressed using 18mm single punch (Korsch XP1), milled (Erweka) and sieved with 0.68mm sieve.

Average tablet weight was 555.5mg, using a compaction simulator (Stylcam 200R) 11mm flat faced Euro B punch for pressing. Formulations were pressed at different compaction forces; 15, 20, 25, 30, 38 and 43kN to understand and characterize formulations as a function of each compaction force, therefore obtain the optimum tablet formulation. Tablets were controlled for weight variation, thickness and hardness for evaluation.

RESULTS AND DISCUSSION:

Results in Fig. 1 indicate that formulations reached optimum breaking force from 25kN. Optimun compaction force was determined as 30kN. Table 2 shows hardness and thickness results of DG-45-1 and DG-45-2 formulations. DG-45-2 is seen to have optimum tabletability profile as a result of its composition.

Fig.1: Comparison of Breaking Force profiles of different formulations.

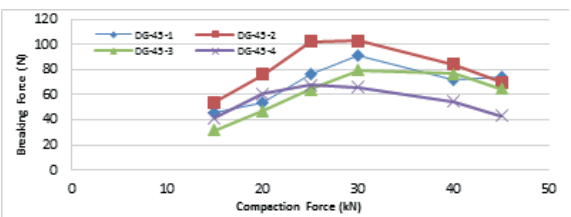


Table 2: Effect of compaction force

Tablet Controls	DG-45-1	DG-45-2	COMPACTION FORCE (kN)
Hardness (N)	45±0,299	54±0,208	15
Thickness (mm)	4,20	4,26	
Hardness (N)	54±0,321	76±0,361	20
Thickness (mm)	4,13	4,15	
Hardness (N)	77±0,252	102±0,306	25
Thickness (mm)	4,05	4,07	
Hardness (N)	91±0,2	103±0,153	30
Thickness (mm)	3,99	4,01	
Hardness (N)	72±0,416	84±0,436	38
Thickness (mm)	3,9	3,91	
Hardness (N)	74±0,321	70±0,265	43
Thickness (mm)	3,86	3,86	

CONCLUSION:

With compaction simulator its possible to define the mechanical properties and optimum tabletability profile for designed formulations.

REFERENCES:

1. Paul S, Sun CC. Int.J.Pharm. 524 (2017) 111-120.
2. Mangal H, Kirsolak M, Kleinebudde P. Int.J.Pharm. 503 (2016) 213-219.

P-336: IN VITRO EVALUATION OF ANTIOXIDANT & CYTOTOXICITY ACITIVITIES OF AL2O3 NANOPARTICLES, BLACK CUMIN OIL AND CO-ENZYME Q10 ON MCF-7 CELL LINE

[1] Sahin, NO., [1] Cavdar, B., [2] Cetin, B.,[3] Sirin, S.

[1] Mersin University, Faculty of Pharmacy, Department of Pharmaceutical Biotechnology, Mersin, Turkey

[2] Mersin University, Faculty of Pharmacy, Department of.Pharmaceutical Technology, Mersin, Turkey

[3] Mersin University, Facuty of Medicine, Department of Internal Medicine, Mersin.

INTRODUCTION:

Breast cancer is the second leading cause of cancer death in Turkish women. It's important to find a less toxic, but more effective way of treating breast cancer patients. Antioxidants such as cumin oil, co-enzyme Q10, can scavenge free radicals and, thus, decrease the occurrence of oxidative stress induced cell death or damage (1,2). Also, it has been proven that nanoparticles can act as synthetic antioxidants in the body and their enlarged surface area can bind specifically to cancerous cells and, thus, offer an approach for cancer therapy (3-4). Taking all these, information into account, the aim of this study was set to evalaute antioxidant and cytotoxic effect of black cumin oil, co-enzyme Q10, and aluminium oxide (Al2O3) nanoparticles, using MCF-7 cancer cell line.

MATERIALS AND METHODS:

Nanoparticles were synthesized by Nanografi, METU. Co-enzyme Q10 and black cumin oil were from Turkish market. The antioxidant activity of all substance under investigation was evaluated by DPPH free radical scavenging assay (3). The cytotoxic effects were investigated on MCF-7 after incubation for 24 h, 48 h and 72 h using MTT assay.

RESULTS:

It is evident from the results (DPPH scavenging activity) that nanoparticles (%28.31 ± 1.12), black cumin oil capsules (%41.3 ± 1.42), and co-enzyme Q10 (%32 ± 1.56) exhibited potent antioxidant activity. Nanoparticles showed sginificant cytotoxict effect alone and in combination with co-enzyme Q10 and black cumin oil (Figure 1).

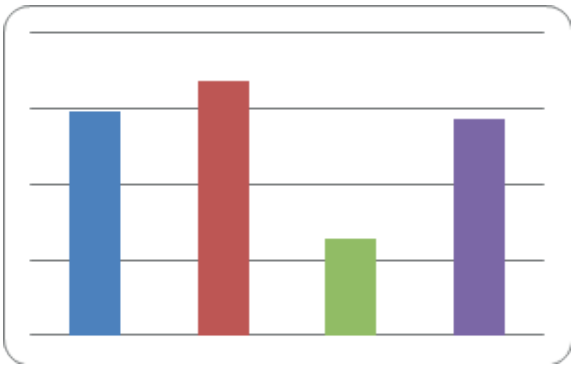


Figure 1. IC50 values for tested substances (nanoparticles, K1: nanoparticles + Co-enzyme Q10, K2: nanoparticles + black cumin oil, K3: nanoparticles + Co-enzyme Q10 + black cumin oil.)

CONCLUSIONS:

In conclusion, it can be suggested that combined use of these three substances possesses significant potential application in nanomedicine as a therapeutic tool.

REFERENCES:

1. Young IS, Woodside JV (2001). J. Clin. Pathol., 54: 176–186.
2. Nimse SB, Pal D (2015). RSC Adv, 5:27986-28006.
3. Swamy MK, Akhtar MS, Mohanty SK, Sinniah UR (2015). Spectrochim. Acta A Mol. Biomol. Spectrosc. 151: 939–944.
4. Das D, Nath BC, Phukon P, Dolui SK(2013). Colloids Surf. B, 101: 430–433.

P-337: POLYMERIC MICROPARTICLES AS ANTIDIABETIC CARRIERS; PREPARATION AND CHARACTERIZATION AS PRELIMINARY STUDIES

[1] Siafaka, P., [1] Caglar, ES.,[1] Ustundag Okur, N.

1Istanbul Medipol University, School of Pharmacy, Department of Pharmaceutical Technology, Istanbul, Turkey

INTRODUCTION:

Diabetes mellitus(DM), is a metabolic disorder in which high sugar levels found in blood for a long period (1). Polymeric microparticles by biocompatible and biodegradable polymers such as poly(ε-caprolactone) and poly(butylene adipate) used so as to entrap active molecules and to release them in a controllable manner (2). In this work, Glibenclamide (GLI) was loaded into poly(ε-caprolactone) (PCL) and poly(butylene adipate)(PBAd) in the form of microparticles in order to improve its solubility.

MATERIALS AND METHODS:

PCL and PBAd were prepared as previously reported (2). Poly(vinyl alcohol)(PVA) was used as an emulsifier. Microparticles were prepared by solid-oil-water (s/o/w) emulsification method (3). 100mg of PCL or PBAd were dissolved in 5mL of dichloromethane. 10mg of GLI was added to prepare loaded microparticles. The polymeric solution was inserted dropwise in 20mL of PVA solution (1% w/v) and homogenized for 1min. After that, it was added in 100mL water and left under magnetic stirring till total evaporation of dichloromethane. The microspheres were collected after centrifugation (8000rpm, 10min) and washed three times with distilled water to remove residuals of solvent and PVA. The resulting microspheres were finally dried and then stored at 4oC for further evaluation. The microparticles were characterized via FT-IR, SEM analysis, and hydrolysis studies.

RESULTS:

The microparticles with or without GLI presented a size of 8-12μm. It was found out that PBAd microparticles were of lower diameter than PCL microparticles while drug incorporation seems to enlarge microparticles. PCL microparticles had a porous structure due to the rigorous solvent evaporation (Fig1). FT-IR spectroscopy studies depicted the successful loading of GLI into the polymeric microparticles. Interactions between carriers and drug have not been revealed (Fig2) (3). Hydrolysis study also demonstrated that PCL microparticles are being degraded slower than PBAd microparticles. In vitro release results found analogous to hydrolysis pattern.

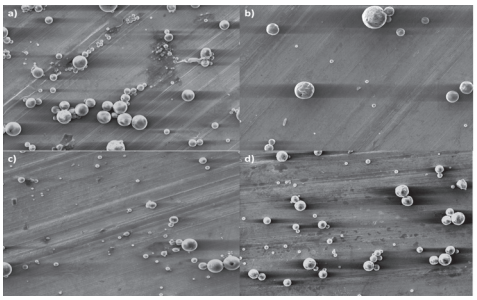


Figure 1: SEM images of microparticles

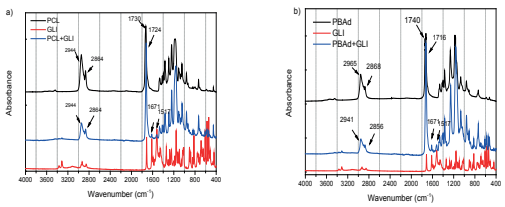


Figure 2: FT-IR spectroscopy results

a) neat PBAd, b) PCL, c) PBAd+GLI d)PCL+GLI

CONCLUSIONS:

It can be concluded that the prepared microparticles seem to be ideal carriers for hydrophobic drugs so as to ensure improved solubility and controlled release pattern.

REFERENCES:

1. Okur ME, Karantas I, Siafaka P (2017). ACTA Pharm Sci 55 :1.
2. Siafaka P, Barmbalexis P, Bikiaris D (2016). Eur J Pharm Sci, 88:12-25.
3. Filippousi M et al., (2016). Int J Pharm, 509: 208-218.

P-338: DERMAL FILMS CONTAINING MUPIROCIN: CHARACTERIZATION, EX VIVO PERMEATION AND BIOADHESION STUDIES

[1] Ustundag Okur, N., [1] Hokenek, N., [1] Siafaka, P, [2] Erdal C.

[1]Istanbul Medipol University, School of Pharmacy, Department of Pharmaceutical Technology, Istanbul, Turkey

[2]Istanbul University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Istanbul, Turkey

INTRODUCTION:

Mupirocin (MUP), a topical antibiotic agent is effectively used for treatment of primary and secondary skin infections (1). The aim of this study was to develop and investigate bioadhesion, ex vivo permeation study of MUP film formulations as a dermal therapeutic system for wound healing applications.

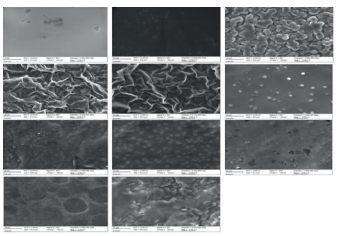
MATERIALS AND METHODS:

MUP loaded films were prepared via solvent casting evaporation method (2). The composition of the film formulations is shown in Table 1. Pure MUP drug, composite films and MUP loaded composite films were characterized by FTIR spectroscopy in order to determine possible interactions between used polymers and MUP. The surface morphology of all formulations were examined by scanning electron microscopy (SEM) at 12 kV. Bioadhesion study was conducted with a texture analyzer. The ex vivo studies were performed for F6, F7, and F8 films using Franz diffusion cell. Mice abdominal skin was used as a model tissue in permeation and bioadhesion studies.

Table 1 : Composition of the films

Ingredients (% w/v)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11
Chitosan	1	1	-	1	1	1	1	1	1	-	-
Sodium Alginate	-		1	1	1	-	-	-	-	1	1
Carbopol	-	-	-	-	-	0,5	0,5	0,5	0,5	0,5	0,5
Glycerine	-	-	-	5	-	5	-	-	10	5	-
PEG 400	5	-	-	-	-	-	5	-	-	-	-
Propylene Glykol	-	5	5	-	5	-	-	5	-	-	5
Mupirocin	2	2	2	2	2	2	2	2	2	2	2

Fig.1. SEM images of MUP dermal films.



RESULTS:

Films had homogeneous appearances and could be easily removed from the petri dishes. FT-IR spectrosocpy studies reveal interactions between polymers in case of unloaded films. When drug was entrapped into the film matrix, possible interactions between MUP and the other ingredients within the formulation did not depict, thus the formulations will present strong stability during its shelf life. SEM morphology revealed that some of the developed formulations (F3, F4, F5) had an interesting architectural structure however most of them don't show any morphology (Fig.1). These results are rational when solvent evaporation technique is applied. The ex vivo permeation results of F6, F7, F8 films were found %12.14+0.951, %9.37+ 2.640, %4.10+1.864 respectively. After bioadhesion study, F6-coded formulation present higher bioadhesive properties than the others.

CONCLUSIONS:

According to the above results, F6-coded formulation found to the most desirable carrier of mupirocin delivery which it is believed to induce wound healing

process. Future studies will involve in vivo examination of the formulation to determine the efficacy of the formulation on wound healing.

ACKNOWLEDGEMENTS:

We would like to thank to Pharmactive Drug for providing MUP.

REFERENCES:

1. Amrutiya et al., (2009). AAPS PharmSciTech, 10(2):402–409.
2. Ustunndağ Okur N et al., (2015). Expert Opinion on Drug Delivery, 12(11):1791–1807.

P-340: EUDRAGİT® S 100 NANOPARTICLES CONTAINING KETOPROFEN LYSNE: PREPARATION AND CHARACTERIZATION

[1] Cinar, Nİ., [2] Ozturk, AA., [2] Yenilmez, E.

[1] Anadolu University, Graduate School of Health Sciences, Department of Pharmaceutical Technology, Eskisehir, Turkey

[2] Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Eskisehir, Turkey

INTRODUCTION:

Ketoprofen lysinate (KL), the water soluble lysine salt of ketoprofen, is one of the most commonly used non-steroidal anti-inflammatory drug (NSAIDs) in the symptomatic treatment of various chronic inflammatory diseases. However, due to its short half-life of 1–2 h, a multiple dose regimen is required. Therefore, KL is an ideal candidate for the development of controlled drug delivery systems which are able to release the drug at a desired rate and in desired amount (1). Eudragit S 100 is an anionic copolymer based on methacrylic acid and methyl methacrylate. It is generally used for the formulation of transdermal patches, nanoparticles, microparticles, solid dispersions and spherical crystals. Eudragit S 100 has been used for various applications such as sustain release, bioavailability enhancement, improvement in micrometric properties (2). According to the aim of this study, KL-containing Eudragit S100 nanoparticles were prepared by double emultion solvent evaporation method (3).

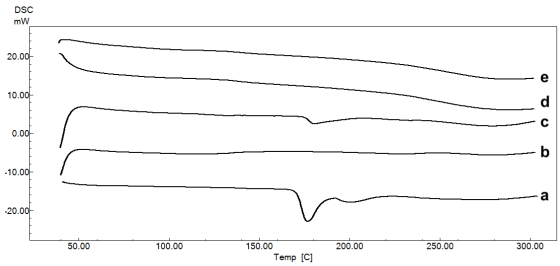
Material and Methods: KL is kind gift from Berko İlaç (Istanbul/Turkey). Eudragit S100 was obtained from Evonik (Germany). Formulations were prepared by double emulsion solvent evaporation method. Particle size (PS), poly dispersity index (PDI) and zeta potential (ZP) measurements were performed on freshly prepared samples using a Malvern analyzer. The entrapment efficiency (EE%) was performed with HPLC with reversed-phase column and also thermal analysis and FT-IR analysis were performed.

RESULTS:

Table 1. Result of PS, PDI, ZP and EE% (n=3)

Code	PS (nm)	PDI	Zeta potential (mV)	EE%
I-Blank	99,07 ± 2,69	0,13 ± 0,05	24,33 ± 0,40	-
I-KL	141,77 ± 1,85	0,47± 0,02	16,43 ± 1,27	%76,537 ± 2,785

Figure 1. a: KL, b: Eudragit® S 100, c: Physical mixture, d: I-Blank, e: I-KL



CONCLUSIONS:

Characterization studies suggest that the active agent is successfully loaded into the polymeric nanoparticle system. In future studies, release experiments will be conducted to determine the release characteristics of the formulations.

REFERENCES:

1. Cerciello A, et al. (2016). Drug development and industrial pharmacy, 42(12), 2063-2069.
2. Patra CHN, et al. (2017). Pharmaceutical significance of Eudragit: 3(1), 33-45.
3. Zafar N, et al. (2016). Materials Science and Engineering: C, 61, 85-96.

P-341: FACTORIAL DESIGN AND DEVELOPMENT OF PLGA MICROPARTICLES FOR PROTIEN DELIVERY SYSTEM

[1] Yurtoglu K., [1] Arslan A.,[1] Ozhan G.,[1] Devrim B., [2] Nemutlu E.,[1] Saka O.M., [1] Bozkir A.

[1] Ankara University, Department of Pharmaceutical Technology, Ankara, Turkey

[2] Hacettepe University, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Several scientific hurdles still have to be overcome before preparing drug delivery systems. One of them is to develop a safe and an efficient protein delivery system. Here, we have employed factorial design to optimize the production of poly(lactic-co-glycolic acid) (PLGA) microparticles for protein delivery. A 2 x 4 full-factorial experimental design was used for the optimization of the formulations. The variables were defined by the components of the formulation: amount

of albumin (BSA), type of PLGA, mixing aparatus and type of solvent at two levels (-1, 1) with 2 extra repated points. Formulations were prepared by varying the selected points and several properties were tested, including their encapsulation efficiency, particle size and zeta potential value.

MATERIALS AND METHODS:

Eighteen formulations of PLGA microspheres containing BSA were fabricated using a spontaneous modified single-emulsion/solvent evaporation method (1). Briefly 200 mg of PLGA were dissolved in 10 mL of 4:1 DCM:Acetone and mixed with 300 mL of BSA in water. Mixing formed a clear, single-phase solution that was subsequently added to 200 mL of 5% (w/v) PVA in water. The emulsion formed spontaneously and was stirred for 3 h at room temperature. Particles were then centrifuged, washed five times with water, and lyophilized.

RESULTS:

The single-emulsion/solvent evaporation technique we use for the preparation of microparticles in this study is a very useful technique in which microparticles are readily obtainable and the production method is easy to scale up (2). The possible formulation parameters affecting the preparation of the microparticles were optimized to achieve the optimum BSA concentration. In this study, it was found that formulations were produced with small particle size, in the range of 80.98–263.4 μm. A high percentage of the DCM increases the polymer load in the aqueous medium during the emulsification process. Zeta potential is the estimate of the surface charge that particles gain in the dispersed state. When the zeta potential values of nanoparticles are close to ±30 mV, the colloidal systems show no aggregation and they form stable dispersions that depends on the repulsion forces between particles. In this study, the zeta potential values of formulations ranged between -5.33 and -25.66 mV.

CONCLUSIONS:

BSA loaded PLGA microparticles were successfully prepared and optimized with 24 factorial design study. The optimized formulation has been found that BSA is effectively encapsulated in microparticles with 150 μm size and above -20 mV.

REFERENCES:

1. Guarecuco, R, Lu J, McHugh K.J, Norman JJ, Thapa, LS, Lydon E, Jaklenec A (2017). Vaccine. 2017.05.094
2. Bozkır, A., Saka O.M. (2005). Il-farmaco, 60 (10), 840-846.

P-342: PREPARATION AND CHARACTERIZATION OF SEMI-SOLID FORMULATIONS CONTAINING LOCAL ANESTHETIC AGENTS

Urfa E., Sayiner O., Arisoy S., Comoglu T.

Ankara University, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

The most commonly used dermal analgesics are lidocaine, tetracaine, prilocaine, or combinations thereof, and the most common topical anesthetic which is regarded as the gold standard is EMLA cream, but it requires occlusion and its effect has a short duration. The object of this study was to develop topical cream and gel formulations of lidocaine-tetracaine (LT) combination with a suitable consistency, and to maintain an effective pain alleviation for a longer duration with a faster onset of action that may be an alternative to EMLA in the drug market.

MATERIALS AND METHODS:

Two different type of formulations of LT combination; a water-in-oil (w/o) emulsion and an emulgel thickened with Carbomer 974 were manufactured. Rheological and pH measurements, quantitative analysis (1) and in vitro studies using Franz diffusion cell at pH=7,4 (2) were performed at day 1 (t0), and formulations were subjected to 25°C/60% RH for 30 days for stability studies. All controls were done at day 30 (t30) to determine the changes in the formulations.

RESULTS:

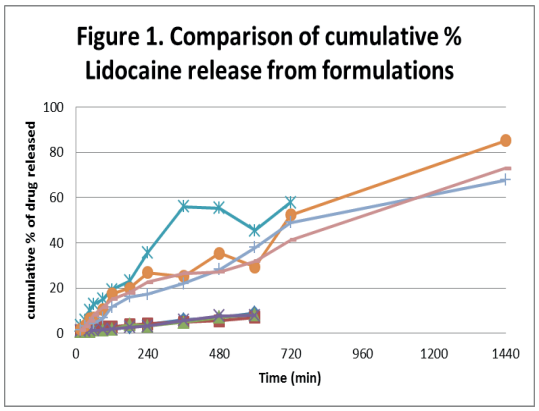
All formulations were white in appearance, homogeneous and odorless after inspection. The emulgels' pH levels changed between 7,2-7,7 at t0, and 8,2-8,9 at t30, respectively. The w/o cream and emulgel formulations showed shear thinning thixotropic behaviour at t0, and rheologic behaviour did not change at t30. The yield percentage of lidocaine was 65-100%, and tetracaine was 45-100% in emulgels, and 39-79% and 47-67% in creams according to quantitative analysises. It has been shown that LT release was faster in emulgel formulations (Figures 1 and 2), and tetracaine release had a longer duration.

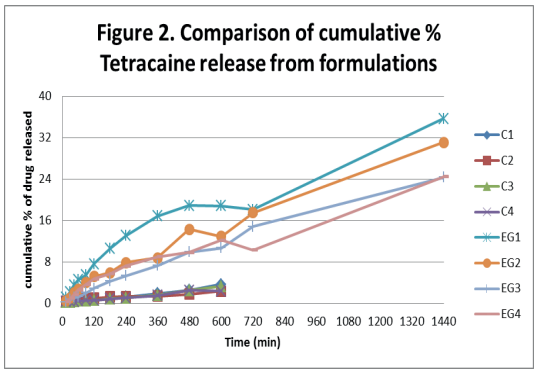
CONCLUSIONS:

Cream and gel formulations of lidocaine-tetracaine (LT) combination with a suitable consistency, pH level and longer duration of action have been manufactured. With conducted studies, it can be interpreted that these formulations can maintain pain alleviation for longer because of tetracaine's release profile.

REFERENCES:

1. Kang L & Jun HW (2003). Drug development and industrial pharmacy, 29(5), 505-512.
2. Olejnik AG (2012). Journal of pharmaceutical sciences, 101(11), 4032-4045.





P-343: ANTI-PROLIFERATIVE EFFECT OF NOVEL MELOTONIN ANALOGS ON BREAST CANCER CELLS

[1] Onar, O., [2] Telkoparan Akillilar, P., [3] Durgun, K., [3] Suzen, S., [1] Yildirim, O.

[1]Ankara University, Faculty of Science, Department of Biology, Ankara, Turkey

[2]Yuksek Ihtisas University, Faculty of Medicine, Department of Medical Biology, Ankara, Turkey

[3]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

INTRODUCTION:

Melatonin is an indolic hormone mainly synthesized and secreted from the mammalian pineal gland. Melatonin production is regulated by photoperiod, which is repressed by light but induced at night in response to darkness (1). Melatonin has been shown cytoprotective effect in normal cells and it inhibits growth of a variety of cancer cells, both in physiological and pharmacological concentrations (2). The therapeutic potential of novel melatonin analogs motivated us to investigate their ability to inhibit proliferation in breast cancer cell lines (MDA-MB-231).

MATERIALS AND METHODS:

Human breast cancer cell lines MDA-MB231 were cultured in DMEM high glucose medium, supplemented with 10% fetal bovine serum, 2 mM L-Glutamine and 1% Penicillin/Streptomycin. MDA-MB231 cells were seeded in 96-well plates and incubated at 37°C with 5% CO2 humidified atmosphere. 24 hours later, cells were treated with 0.1% DMSO dissolved in culture medium or with different doses of melatonin and 19 different melatonin analogs diluted in 0.1% DMSO and cultured for 24 and 48 hours. The cell viability and proliferation were investigated with colorimetric MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] assay, according to the manufacturer's protocol. 10 µL MTT (5 mg/mL dissolved in phosphate-buffered saline) was added to each well and plate was incubated for 4 h. MTT containing media were removed, and the purple formazan crystals were dissolved in 100 µl dimethyl sulfoxide. The absorbance was recorded on a microplate reader at the wavelength of 570 nm. The experiments were performed in triplicate and repeated three times.

RESULTS:

The sensitivity of human breast cancer cell line, MDA-MB-231, to the melatonin and newly synthesized 19 different melatonin analogs was assessed by using a MTT cellular survival assay. The experiments revealed that melatonin and new melatonin analogs inhibited the growth of MDA-MB231 breast cancer cells in a dose and time dependent manner. In addition, MDA-MB231 breast cancer cells were more sensitive to melatonin analogs KD11, KD12 and KD13 and these analogs displayed the most anti-proliferative and cytotoxic effects at low concentrations (0.5uM) in a shorter time of exposure. These data indicate that novel melatonin analogs are potent inhibitors of human breast tumor cell proliferation.

CONCLUSIONS:

We demonstrated that novel melatonin analogs inhibit the growth of breast cancer cell lines in vitro and suggesting the oncostatic / cytotoxic role of these compounds.

REFERENCES

1. Brainard GC et al., (2001). Journal of Neuroscience, 21:6405–6412.

2. Bizzarri M et al., (2013). Expert Opin Ther Targets, 1483–1496.

P-344: PREPARATION AND IN-VITRO CHARACTERIZATION OF AMPICILLIN SODIUM-LOADED ALGINATE BEADS FOR ORAL ANTIBIOTIC TREATMENT: A PRELIMINARY STUDY

Duman, S., Sevinc Ozakar, R., Ozakar, E.

Ataturk University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Erzurum, Turkey

INTRODUCTION:

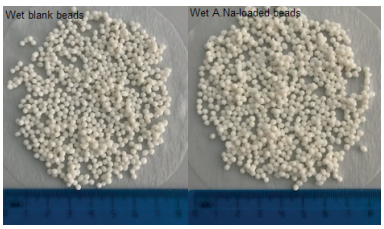
Oral drug delivery is the most popular and convenient method for decades. The high level of patient compliance in taking oral dosage forms is due to the ease of administration, patient compliance, flexibility in formulation and handling of these forms (1). Antibiotics such as ampicillin sodium (A.Na) are commonly used for systemic therapy as well as for gastric or intestinal infections. Among the semi-synthetic penicillins, ampicillin has found widespread use owing to its broad spectrum of activity (2). It is acid resistant and therefore can be given orally (3). The aim of this study is to develop calcium alginate beads with improved properties for controlled delivery of A.Na.

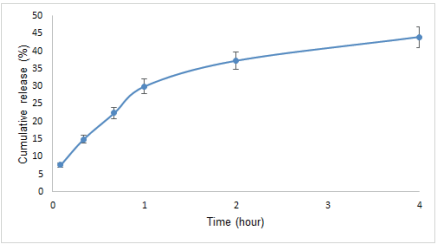
MATERIALS AND METHODS:

A.Na (a generic drug in pharmacies, Turkey), sodium alginate (Alfa Aesar, Germany). Calcium alginate beads containing A.Na were prepared by ionotropic gelation method. For characterization study, encapsulation efficiency (EE, %), drug loading (DL, %), yield (%), surface morphology, particle size, and in vitro release were evaluated. The beads were failed in buoyancy test. The particle sizes of the beads were measured with an manual calliper. An incubation method was used for determination of A.Na release from beads in pH 1.2 HCl buffer at 37 °C for 4 hours.

RESULTS:

Digital photographs of wet blank and A.Na-loaded beads show the spherical morphology. In vitro release of A.Na into HCl buffer from the beads was slow and sustained but insufficient. The results of the characterization studies of beads are showed below.





		EE (%) n=3	DL (%) n=3	Yield (%) n=3	PS* (mm) n=75
Blank Beads	Mean	-	-	81.23	1.40
	SD*	-	-	1.36	0.20
A.Na-Loaded Beads	Mean	25.09	3.92	80.30	1.57
	SD	4.30	0.74	5.40	0.28

**PS: Particle size of dry beads, SD: Standard deviation.*

CONCLUSIONS:

Experiments were done to establish the optimum conditions for the preparation of homogenous and spherical beads with a smooth surface. A.Na beads provides a controlled release formulation with sustained-release properties for prolonged periods. But in order to improve the EE, DL or in vitro release results, further studies should be performed.

ACKNOWLEDGEMENTS:

This study was supported by a grant of BAP (TAB-2017-6334).

REFERENCES:

1. Patil H, Tiwari RV, Repka MA (2016). AAPS PharmSciTech, 31:65-71.
2. Nishi KK, Antony M, Jayakrishnan A (2007). The Journal of pharmacy and pharmacology, 59:485-493.
3. Anal AK, Stevens WF (2005). International journal of pharmaceutics, 290:45-54.

P-345: NOVEL GASTRORETENTIVE DRUG DELIVERY SYSTEMS: PREFORMULATION STUDIES OF AMPICILLIN SODIUM-LOADED GELISPHERES

Ince, AY., Sevinc Ozakar, R., Ozakar, E.

Ataturk University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Erzurum, Turkey

INTRODUCTION:

One of the most feasible approaches for achieving a prolonged and predictable drug delivery profiles in gastrointestinal tract with different mechanisms is to control the gastric residence time using gastroretentive drug delivery systems that offer a new and better option for drug delivery (1). Gelispheres are spherical crosslinked hydrophilic polymeric drug delivery systems capable of extensive gelation and

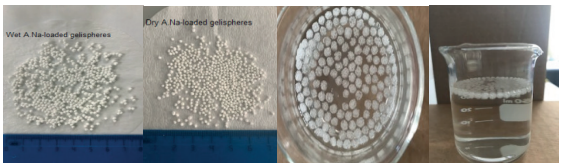
swelling characteristics in simulated biological fluids (2). Ampicillin sodium (A.Na), being a potent, broad spectrum antibiotic, is commonly used for systemic therapy as well as locally for gastric or intestinal infections (3). The aim of this study is to develop cellulose gelispheres with improved properties for gastroretention of A.Na.

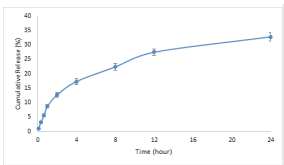
MATERIALS AND METHODS:

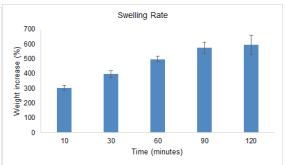
A.Na (a generic drug in pharmacies, Turkey), synthetic cellulose (Doga Ilac, Turkey). Gelispheres containing A.Na were prepared by ionotropic gelation method. For characterization study, encapsulation efficiency (EE, %), drug loading (DL, %), yield (%), surface morphology, particle size, floating, swelling and in vitro release were evaluated. The particle sizes of the beads were measured with an manual calliper. An incubation method was used for determination of A.Na release from gelispheres in pH 1.2 HCl buffer at 37 °C for 24 hours.

RESULTS:

Digital photographs of wet/dry A.Na-loaded and floating gelispheres show the spherical morphology. All of the gelispheres were floating for 5 days. The other results of the characterization studies of beads are showed below.







		EE (%) n=3	DL (%) n=3	Yield (%) n=3	PS* (mm) n=75
Blank Beads	Mean	-	-	39.16	1.98
	SD*	-	-	1.84	0.21
A.Na-Loaded Beads	Mean	18.55	2.78	39.17	1.96
	SD	1.03	0.04	1.84	0.73

**PS: Particle size of dry beads, SD: Standard deviation.*

CONCLUSIONS:

Gastroretentive drug delivery systems have emerged as an efficient means of enhancing the bioavailability and controlled delivery of many drugs. These systems might be beneficial over the conventional oral dosage forms for therapeutic efficacy of A.Na.

REFERENCES:

1. Anandam S, Srilakshmi N, Rani PS (2016). IAJPS, 3:209-218.
2. Patil P, Chavanke D, Wagh M (2012). International Journal of Pharmacy and Pharmaceutical Sciences, 4:27-32.
3. Anal AK, Stevens WF (2005). International Journal of Pharmaceutics, 290:45-54.

P-346: PREPARATION AND CELL CULTURE STUDIES OF DEXAMETHASONE NANOPARTICLES FOR ORAL CANCER CHEMOPREVENTION

[1] Rencber, S., [2] Aydin Köse, F., [1] Karavana, SY.

[1]Ege University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Izmir, Turkey

[2]Ege University, Faculty of Pharmacy, Department of Biochemistry, Izmir, Turkey

INTRODUCTION:

The aim of this study was to prepare and evaluate cell culture of Dexamethasone (DEX) loaded PLGA nanoparticles (NPs) for oral cancer chemoprevention.

MATERIALS AND METHODS:

The DEX loaded PLGA NPs were prepared by a emulsification/solvent evaporation method (1). Cytotoxicity potential of the NPs was evaluated by MTT assay (2). Human kidney proximal tubular epithelial cell line (HK-2, ATCC) were cultured in 10% fetal bovine serum (FBS) supplemented DMEM: F12 medium. Mouse embryo fibroblast cell line (NIH-3T3) were grown in 10% FBS supplemented DMEM. Cells were maintained at 37°C in a humidified atmosphere at 37 ºC. Cells were plated in 96-well plates at a density of 5×103 cells/ well and incubated in a humidified atmosphere for 24 hours for cell attachment. Then, the cells were treated for 48 hours with a 1:1,000 dilution of the tested formulation. Cells treated with medium only used as a control. After removing the medium, cells were washed with PBS. Medium and MTT solution were added to each well to determine the cell viability. After incubation, blue-colored formazan crystals were dissolved in dimethyl sulfoxide. The absorbance of the formazan solution was measured in a plate reader. The ratio of the absorbance of treated samples to the absorbance of control was expressed as % cell viability. Cell survival was expressed as the percentage of formazan absorbance. Statistical analysis was conducted by ANOVA followed by Tukey's test.

RESULTS:

The NPs were prepared successfully. Cytotoxicity is a key factor while choosing a suitable drug delivery carrier. It was determined that NPs caused a significant increase in cell viability of HK-2 and NIH-3T3 cells compare to control cells. On the other hand, it was not found any cytotoxic effect of the NPs to HK-2 cell nor 3T3 cell. These cytotoxicity results signified that NP had the potential to be used as a carrier for DEX delivery.

CONCLUSIONS:

The objective of the present work of formulation and evaluating cell culture studies of DEX loaded NPs has been achieved with success.

ACKNOWLEDGEMENTS:

This study was supported by a research grant from Ege University (16/ECZ/015). We would like to acknowledge E.U. Pharmaceutical Sciences Research Center for enabling us to use its laboratory instruments.

REFERENCES:

1. Sun C et al. (2015). International Journal of Nanomedicine, 10: 3567-3579.
2. Mosmann T (1983). J Immunol Meth., 65:55-63.

P-347: A COMPERISON OF PLGA NANOPARTICLE PREPARATION METHODS FOR BEVACIZUMAB ENCAPSULATION

[1] Akbas, S., [2] Ultav, G., [3] Tonbul, H., [4] Sahin, A., [4] Capan, Y.

[1] Hacettepe University, Department of Pharmaceutical Technology, Ankara, Turkey

[2] Hacettepe University, Department of Nanotechnology and Nanomedicine, Ankara, Turkey

[3] Inonu University, Department of Pharmaceutical Technology, Malatya, Turkey
4ILKO Pharmaceuticals, Istanbul, Turkey

INTRODUCTION:

Bevacizumab is a recombinant monoclonal antibody that approved by Food and Drug Administration (FDA), for treatment of patients with metastatic renal cell cancer, non-small-cell lung cancer, metastatic colorectal cancer, epithelial ovarian and fallopian tube cancer in the USA and Europe (1). The nanotechnological approaches have emerged to maintain antibody stability, achive controlled release and targeted delivery of the antibody via encapsulation of antibodies into polymeric nanoparticles (2). In the studies conducted, researchers are focused on PLGA since it is an biodegredable and bioavailable FDA approved polymer (3). Encapsulation efficiency of the antibody alters with the preparation method of nanoparticles. In this study, bevacizumab loaded nanoparticles were prepared by two different methods and characterization studies were performed.

MATERIALS AND METHODS:

Bevacizumab, Altuzan®, Shikari Bevacizumab Elisa Kit, PLGA-PEG (Sigma-Aldrich), Pluronic F-68 (Cellgro)

Methods: Double Emulsion Method and modified solvent diffusion technique were compared (4-5). Nanoparticle characterizations were performed with Zetasizer Nano ZS and Elisa Kit.

RESULTS:

The average particle sizes of the nanoparticles obtained by the modified solvent diffusion technique and double emulsion method were 250 nm and 120 nm respectively. It was found that encapsulation activities of the nanoparticles obtained by the modified solvent diffusion technique (70%) were higher than the encapsulation activities of the nanoparticles obtained by the double emulsion method (20%).

CONCLUSIONS:

It is crucial to maintain the stability of antibodies during nanoparticle preparation since stress factors such as sonication can disrupt antibody stability and decrease encapsulation efficiency. In this study, it was pointed out that modified solvent diffusion technique is a better alternative for antibody encapsulation than double emulsion method.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (1003) and ILKO Pharmaceuticals

REFERENCES:

1. Monk BJ et al. (2017). Gynecologic Oncology Research and Practice, 4:7
2. Sousa F et al. (2017). Expert Opinion on Drug Delivery, 17:10
3. Sharma et al. (2016). Trends in Analytical Chemisty, 30:40
4. Varshochian R et al. (2015). Journal of Biomedical Materials Research - Part A, 103:10
5. Csaba N et al. (2006). Journal of Controlled Release, 113:2

P-348: DEVELOPMENT OF MONO AND BILAYERED BIOADHESIVE FILM FORMULATIONS FOR ORAL MUCOSAL DRUG DELIVERY

Timur, SS., Yüksel, S., Senel, S.

Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Various delivery systems have been developed for delivery of drugs into oral cavity for local effect or across oral mucosa for systemic effect. Major limitation in developing an oral mucosal delivery system is the movement of the tongue as well as salivation. For an effective drug delivery, systems based on bioadhesive polymers have been investigated to enhance the retention time of the system in contact with the tissue and also provide prolonged release of the drug. Chitosan, which is a bioadhesive and bioactive polymer, has been widely utilised in different forms for local delivery into oral cavity.

MATERIALS AND METHODS:

In this study, chitosan based mono and bilayered films were developed for oral mucosal delivery. The monolayer films were prepared using solvent casting method, and bilayered films using double-casting method. Cefuroxime axetil (5 % w/w), which is a wide-spectrum antibiotic was used as model drug. Morphology of the formulations was examined using scanning electron microscopy. Mechanical (tensile strength) and physical properties (water absorption capacity, bioadhesion, thermal behaviour) as well as disintegration properties of the formulations were investigated. In vitro drug release studies were performed using Franz diffusion cells.

RESULTS:

Homogenously dispersed mono and bilayered films were obtained with chitosan. All formulations incorporated with drug remained intact without disintegration up to 5 to 6 h. DSC thermograms confirmed that the drug was consistently incorporated into the formulations. With monolayer films, bioadhesion (13.71±2.73 (mJ/cm2) was decreased in presence of drug, whereas with bilayered films, bioadhesion was found to increase (105.3±23.4 (mJ/cm2). Water absorption capacity of the bilayered films (288.4±8.7%) was found to be higher than that of monolayer films (111.4 ±14.9 %). A prolonged drug release was obtained up to 5 h.

CONCLUSION:

Chitosan based films were developed successfully with suitable bioadhesive property and disintegration time which would enable the system to remain attached on the application site and release drug in a prolonged fashion.

ACKNOWLEDGEMENT

Authors are thankful to IE Ulagay-Menarini, İstanbul, Turkey for providing cefuroxime axetil, and Koyo Company, Japan for providing chitosan as a generous gift.

P-349: COMPARISON OF DIALYSIS VS SAMPLE AND SEPARATION METHODS FOR IN VITRO RELEASE DETERMINATION OF LEVODOPA FROM NANOPARTICLES

Arısoy, S., Sayıner, O., Comoglu, T.

Ankara University, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

The aim of the present study was to compare dialysis (DM) and sample and separation (SS) methods for determining in vitro release of levodopa from nanoparticles. Nanoparticles were prepared by double emulsion-solvent evaporation method, using methylene chloride as an organic solvent and polyvinyl alcohol as the surfactant. Samples were withdrawn and drug concentration was determined using HPLC. The rate and extent of drug release from nanospheres was dependent on the drug/polymer ratio, and drug loading of nanoparticles. The $f1$ and $f2$ statistics were used to compare the two methods (1).

MATERIALS AND METHODS:

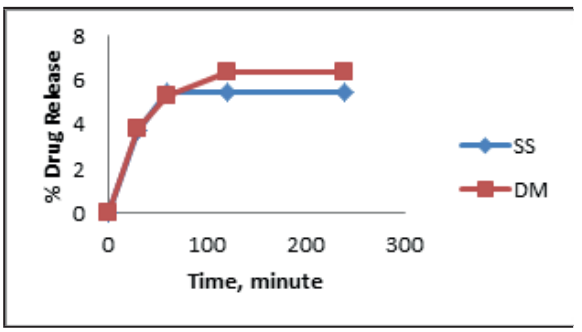
In vitro release studies were performed by incubating nanoparticles (equavalent to 45 µg levodopa) in 5 ml of buffer, pH 4,5. The tubes were stirred continuously at 37± 0.5 °C in a water bath nd shaken horizontally at 100 rpm. To practice the SS method the tubes were taken out of the water bath and centrifuged. The precipitated nanoparticles were resuspended in 5 ml of fresh buffer. Unlike SS method, in DM method nanoparticles were suspended in 0,5ml of buffer solution in a dialysis bag than placed in 4,5 mL buffer. At predetermined time intervals all media replaced with fresh buffer solution.

RESULTS :

Table 1. $f1$and $f2$ statistics for the dissolution profile using the DM as reference and the SS as test model

	SS method	DM method
Time (minute)	Test Model, Drug Release (%)	Reference Model, Drug Release (%)
30	3,73±0,03	3,81±0,01
60	5,45±0,02	5,33±0,05
120	5,45±0,02	6,38±0,01
240	5,45±0,02	6,38±0,01
	$f1$	6,02
	$f2$	95,38

Figure 1. Comparative release pattern of levodopa from nanoparticles using the DM and SS methods.



CONCLUSIONS:

DM and SS methods gave similar shapes of in vitro release profiles at acceptable precision (‹10%,CV). The SS method tended to show faster release rates from formulations than those observed using dialysis bag (Table 1). The difference between DM and SS methods in the release kinetics did not reach significance (f1 < 15 and f2 > 50).

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK.

REFERENCES:

1. Shazly G, Nawroth T, Langguth P(2008), Dissolution Technologies.

P-350: PREPARATION AND CHARACTERIZATION OF NANOFIBERS CONTAINING ORNIDAZOLE FOR BUCCAL APPLICATION

Tort,S., Yıldız, A., Tugcu Demiroz, F., Tuncel, E., Acarturk F.

Gazi University, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Gingivitis is a common and mild form of periodontal disease that causes irritation, redness and swelling of gingiva(1). Ornidazoles, as a nitroimidazole derivative, are antibiotics that are widely used to treat anaerobic infections(2). Nanofibers are suitable for a wide range of applications owing to their capability for accepting various types of loading materials in their structures, such as antibiotics, anticancer drugs, nucleic acids, and proteins(3). The aim of this study, was to develop buccal application of ornidazole for treatment of gingivitis by loading ornidazole into nanofibers.

MATERIALS AND METHODS:

Polyvinylpyrolidone (PVP) solutions at different concentrations (10, 12.5 and 15%,w/v) in ethanol were prepared, and the nanofibers were produced by electrospinning technique using these solutions. The ornidazole loaded solutions (0.5%, w/v) at different PVP concentrations were compared in terms of viscosity, conductivity and surface tension. The ornidazole-loaded nanofibers were characterized by fourier transform infrared spectroscopy (FTIR), differential scanning calorimetry (DSC) and scanning electron microscopy (SEM). Mechanical properties of nanofibers were investigated using a texture analyzer.

RESULTS:

An increase in the polymer concentration from 10 to 15% led to a decrease in the solution conductivity and surface tension values and an increase in the solution viscosity values. Similar results were observed in ornidazole-loaded polymer solutions. DSC and FT-IR analyses suggest that ornidazole is present in the nanofibers and there were no interactions between ornidazole and PVP. The increase of polymer concentration from 10 to 15% led to an increase in average nanofiber diameter. The average diameters of the ornidazole-loaded nanofibers were found to be 680, 1350 and 1320nm for PVP concentrations of 10, 12,5 and 15%, respectively. The developed buccal nanofiber comprises with a contact angle of 0°, a tensile strength of between 1,67-5,12MPa and an elongation at break value of 14-19% for PVP concentrations between 10-15% (Fig.1). Entrapment efficiencies of ornidazole in the nanofibers were found to be 57, 83 and 71µg/cm2 for PVP concentrations of 10, 12,5 and 15%, respectively. PVP concentration directly affected nanofiber diameter and mechanical properties of nanofibers.

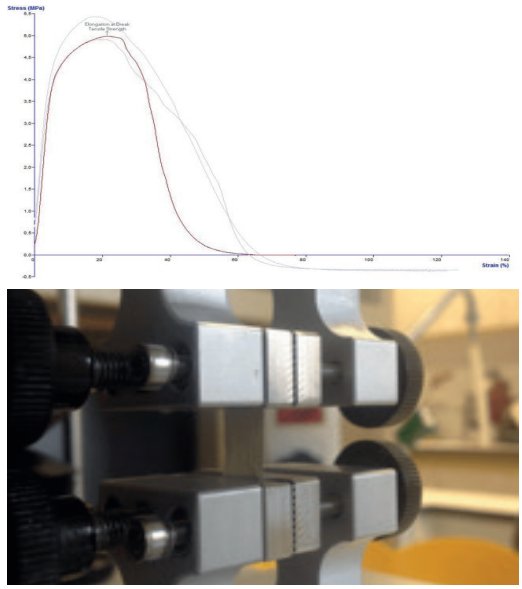


Figure 1. Stress-strain curves of ornidazole-loaded PVP nanofibers

CONCLUSIONS:

In the present study, ornidazole-loaded nanofibers were successfully developed for the treatment of gingivitis. The antibacterial efficacy of ornidazole-loaded nanofibers could offer improved efficacy in the treatment of gingivitis.

REFERENCES:

1. Adinarayan R et al., (2016). Journal of Dental Sciences, 2(1):47-51.
2. Mastiholimath VS et al., (2006). Indian Journal of Pharmaceutical Sciences, 68(1):68-71.
3. Tort H et al., (2017). Journal of Drug Delivery Science and Technology, 41:317-324.

P-352: PH-DEPENDENT DISSOLUTION BEHAVIOR OF A WEAKLY BASIC BCS CLASS II DRUG, CLOPIDOGREL

Olgac, S., Yildiz, A., Saar, S., Kodan, E., Incecayir, T.

Gazi University, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

The aim of this study was to investigate the pH-dependent dissolution of a weakly basic BCS II (low-solubility and high-permeability) drug, clopidogrel and compare the in vitro dissolution of its innovator and three generic products to assess the in vivo dissolution and intestinal permeability of this oral antiplatelet agent.

MATERIALS AND METHODS:

Clopidogrel bisulfate was kindly supplied from Deva Holding(Turkey). Four commercial IR tablets of 75 mg clopidogrel were purchased from local market. Dissolution tests were carried out using a Varian VK7000 dissolution apparatus(USA). The reference and test tablets were placed in 900 mL of dissolution media at 37oC using USP Apparatus II at 50 rpm. pH 1.2 HCl, pH 4.5 acetate and pH 6.8 phosphate buffers were used as dissolution media. An aliquot of medium was withdrawn at predetermined time intervals, and an equivalent amount of fresh medium was added. Withdrawn samples were filtered using a 0.45 µm filter and analyzed at 220 nm spectrophotometrically. All dissolution experiments were carried out in triplicate and mean cumulative percentages of drug dissolved from the tablets were plotted against time. f2 similarity test was used to compare dissolution profiles of reference and test products. Dose numbers(DO) were calculated. The un-ionized drug fraction(fu) at a given pH was calculated using Wagner and Sedman's equation (3).

RESULTS:

DO at pH 1.2, 4.5 and 6.8 are 0.010, 0.170 and 39.1, respectively. At least 85% of the labeled amount was dissolved within 30 min for reference and all test products except one test (86% dissolved in 45 min) at pH 1.2. At pH 4.5 and 6.8, drug dissolved from all products were in the range of 78-101% and 37-51% in 90 min. Only one of the test product showed dissolution profile similarity(f2>50) to reference in each case. The un-ionized fraction(fu) of clopidogrel (pKa:4.56, log P:3.9) is nearly zero up to pH 2, and then gradually increases as pH increases giving the sigmoidal profiles around pH 6.5. fu values of clopidogrel in jejunal pH 6.0 and ileal pH 7.4 are high and similar, which may explain our previous data on clopidogrel's high Peff with no regional dependency (4).

CONCLUSIONS:

This study shows that the dissolution of all test and reference products of clopidogrel is likely to be complete in stomach, and entering the upper intestine, it is likely to be present in a supersaturated state, and rapidly absorbed before precipitating at the high pH of the small intestine.

ACKNOWLEDGEMENTS:

The authors would like to thank Deva Holding (Istanbul, Turkey) for kindly providing the drug

substance for research purpose.

REFERENCES:

1. Sheng JJ et al. (2006). European Journal of Pharmaceutical Sciences, 29:306-314.
2. Galia E et al. (1998). Pharmaceutical Research, 15:698-705.
3. Dahan A et al. (2010). Molecular Pharmaceutics, 7:1827-1834.
4. Incecayir T et al. (2016). Pharmazie, 71:472-477.

P-353: FORMULATION AND EVALUATION OF DEXKETOPROFEN MINI TABLETS FOR CHRONOTHERAPY

Ilhan, E., Sahbaz, S., Ugurlu, T., Aldeniz, EE.

Marmara University, Department of Pharmaceutical Technology, İstanbul, Turkey

INTRODUCTION:

Dexketoprofen trometamol is indicated for the management of acute pain including dental pain, dysmenorrhoea and muscular pain and used more than one dose in a day without exceeding 75mg/day (1). In order to increase the patient's compliance and to keep the pain under better control, a novel pulsatile release drug delivery system of dexketoprofen was designed by filling mini tablets into hard gelatine capsule.

MATERIALS AND METHODS:

Dexketoprofen trometamol was purchased from Huangshi Shixing Pharmaceutical Co, Ltd., (China), maize starch from Roquette Pharma (France), microcrystalline cellulose from JRS Pharma (Germany), sodium starch glycolate from DFE Pharma (Germany), glyceryl behenate from Gattefossé (France), Eudragit L 100 and Eudragit S 100 from Evonik Röhm GmbH, (Darmstadt, Germany). Talc, triethyl citrate, acetone and isopropyl alcohol all were in analytical grade.

Mini tablets (1mg dexketoprofen per tablet) were prepared by wet granulation method. As designed for immediate release (IR) and colon targeted drug delivery (CTDD) combination, half of tablets (25 tablets) were coated with pH sensitive polymers (Eudragit L 100 and/or Eudragit S 100) and the other

half remained uncoated. After preparing all tablets, they all (50 tablets) filled into hard gelatine capsule. Drug release test was initiated in a buffer system at pH1.2 (750 ml); after 2 h, the pH was altered to 6.8 (1000 ml) by sodium phosphate solution to mimic the pH in the stomach and colon (2).

RESULTS:

IR formulations were found to have similar dissolution profile with the reference product. As developing CTTD, after trying different processes, spray coating gave better coating performance and dissolution profiles than pan coating.

CONCLUSIONS:

As the formulations are mini tablets, it gave different coating results compared with the basic tablets. Mini tablets were coated more homegenously with spray coating method and it was seen that Eudragit S 100 coating was more resistant than Eudragit L 100 coating to colonic condition.

ACKNOWLEDGEMENTS:

This study was supported by DEVA Holding A.Ş.

REFERENCES:

1. Barbanoj MJ, Antonijoan RM, Gich I (2001) Clinical Pharmacokinetics, 2001; 40 (4): 245-262.
2. Park HJ, Jung HJ, Hob MJ, Lee DR , Cho HR, Choi YS, Jun J, Miwon Son a, Myung J. KangEuropean Journal of Pharmaceutical Sciences 102 (2017) 172–179.

P-354: PREPARATION AND CHARACTERIZATION OF EGF CONTAINING HYDROGEL FORMULATIONS

[1] Dogan, M., [1] Sezer, AD., [2] Sahbaz S., [2] Ugurlu, T.

[1]Marmara University Department of Pharmaceutical Biotechnology, İstanbul, Turkey

[2]Marmara University Department of Pharmaceutical Technology, İstanbul, Turkey

INTRODUCTION:

Wound is known as the impairment of tissue integrity. Wound healing include; homeostasis, inflammation, cell proliferation, extracellular matrix production and wound closure respectively(1,2). Epidermal Growth Factor (EGF) play an important role in dermal wound healing proceses which accelerate the epidermal cell regeneration and stimulate keratinocyte proliferation and migration (3). Chitosan and PVA are widely used in hydrogel formulations for wound healing process. (3,4). Our main goal was to prepare different hydrogel formulations and investigate the mechanical properties and therapeutic efficacy (1,4).

MATERIALS AND METHODS:

Materials: EGF(h), EGF(m), chitosan(m), chitosan(h), PVA, mPEG propiyonaldehyde (MW 5kD) and mPEG propiyonaldehyde (MW 10 kD) was used in our studies. All materials used in this studies are in analytical grade.

Methods: The concentration of chitosan which will form the hydrogel formulation will be determined as 3%.The concentration of PVA, the other polymer to be used, will be determined as 2%(2). EGF Pegylation reaction take places between the aldehyde group of PEG and the α amine moiety in the N-terminal region of the protein and consist of Schiff base moiety. The swelling behavior of the hydrogels is strongly dependent on the gel ionization and the ionic strength around the solution(3).In order to investigate the mechanical properties of hydrogel formulations, TA.XT Plus Texture Analysis (Stable Micro Systems, UK) device and the Texture Exponent software of the device was used(4). Brookfield DV-E viscometer was used to measure the viscosities of the hydrogels(4).

RESULTS

Fig 1: Mechanical Properties of Hydrogels by Texture Analyzer

Formulations	Hardness(N)	Adhesiveness(N.s)	Cohesiveness	Elasticity	Fracturability	Resilience	Compressibility
A1.1	0,039	-0,0282	0,865	0,971	0,017	0,146	0,237
A1.2	0,041	-0,0184	0,839	0,984	0,000	0,313	0,247
D1.1	0,030	-0,0232	0,950	1,247	0,000	0,398	0,221
D1.2	0,038	-0,0206	0,847	0,987	0,017	0,260	0,232
E1.1	0,057	-0,0705	0,835	0,934	0,010	0,271	0,252
E1.2	0,044	-0,0901	0,838	0,931	0,019	0,159	0,240
H1.2	0,052	-0,1024	0,846	0,939	0,018	0,142	0,256

CONCLUSIONS:

The results showed that hydrogels which consist of high molecular weight chitosan is more viscous, adhesive and has more hardness than the hydrogels including medium molecular weight chitosan.

ACKNOWLEDGEMENT

This study was supported by BAPKO (SAG-C-DRP-131216-0537)

REFERENCES:

1. Lee H, Park T. G. (2002) Pharmaceutical Research 19 (6): 845-851.
2. Zhanga D, Zhoua W, Weib B, Wangb X. (2015) Carbohydrate Polymers. 125: 189–199.
3. Ahmed E. M. (2015) . Journal of Advanced Research. 6 :105–121.
4. Sezer AD, Cevher E, Hatipoğlu F, Ogurtan Z, Baş A.L, Akbuğa J. (2008). Biological and Pharmaceutical Bulletin. 31(12): 2326—2333.

P-355: PREFORMULATION STUDIES OF CYCLOSPORINE A NANOSUSPENSION STABILIZED BY HYDROXYPROPYL METHYLCELLULOSE AND SOLUPLUS®

Gulbag, S., Karakucuk, A., Mutlu Agardan, B., Celebi, N.

Gazı University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Cyclosporine A (CsA) is a well-known immunosuppressive agent that has used following organ transplantion (1). Nanosuspensions are colloidal dispersions containing nanoscale drugs stabilized by surfactants and polymeric steric stabilizers. Nanosuspensions are currently very attractive because they can increase the solubility, dissolution and bioavailability of water insoluble drugs (2).

In the present study, CsA nanosuspension was prepared by high pressure homogenization method using Design of Experiment (DoE) approach and in vitro characterization studies including particle size (PS), polydispersity index (PDI), zeta potential (ZP) measurement, surface morphology, differential scanning calorimetry (DSC) were evaluated.

MATERIALS AND METHODS:

Preparation of CsA nanosuspansions using microfluidization technique was performed. Firstly, HPMC and Soluplus® (CsA:stabilizer 1:1, 1:2, 1:4) were used to stabilize the nanosuspension separately. Secondly, the combination of HPMC and Soluplus® (CsA:HPMC:Soluplus® 1:1:0.25, 1:1:0.5) were used to obtain nanosuspension formulation. Stabilizers were dissolved in distilled water and 1% CsA was dispersed in this solution. The Ultraturrax (at 15.000 rpm for 10 minutes) was used to minimize PS of the coarse suspensions. Different homogenization cycles (5, 15, 30) were applied at 30.000 psi process pressure on the microfluidizer to obtain CsA nanosuspensions. 32 (3 levels, 2 factors) full factorial design was applied to optimize the formulations. PS, PDI and ZP values of nanosuspensions were measured after the initial, 1 week and 1 month and compared for short term physical stability. Obtained CsA nanosuspensions were lyophilized for 48 hours and in vitro characterization studies were performed.

RESULTS:

PS values were measured between 700 nm and 1750 nm and ZP values were measured -20 mV with HPMC stabilized nanosuspensions. PS and ZP values were noticed 200 nm and -8 mV with Soluplus® stabilized nanosuspensions respectively. Therefore, combination HPMC and Soluplus® was used to obtain smaller PS and higher ZP values. The PS, PDI and ZP values were found for CsA:HPMC:Soluplus® 1:1:0.5 formulation 366.8±9.6 nm, 0.48±0.02 and -14.4±0.4 mV, respectively.

CONCLUSIONS:

CsA nanosuspensions were successfully obtained using the DoE approach by selecting HPMC and Soluplus® combination as stabilizers.

ACKNOWLEDGEMENTS:

This study was supported by Gazi University Scientific Research Project Foundation (No:02/2017-14). The authors are thankful to Deva Drug Company (Turkey) for providing CsA

REFERENCES:

1. Guada M, Beloqui A, Kumar MNVR, Préat V, Dios-Viéitez MC, Blanco-Prieto MJ (2016). Reformulating cyclosporine A (CsA): Journal of Controlled Release 225: 269-282.
2. Wang L, Du J, Zhou Y, Wang Y (2017Nanotechnology, Biology, and Medicine 13: 455–469.

P-356: CONTROLLED DRUG RELEASE FROM 2-HYDROXYETHYLCELLULOSE-GRAPHENE NANOCOMPOSITE FILMS

Salih Hussein, H., Alemdar, S., Pekel Bayramgil, N.

Hacettepe University, Faculty of Science, Department of Chemistry, 06800, Beytepe, Ankara, Turkey

INTRODUCTION:

Nanotechnology is an engineering science at the atomic and molecular level. It is a scientific discipline in which new nano-sized structures are designed and synthesized, or the existing nano-sized structures are made unique, and these properties are used in new applications. Graphene is the only atomic layer of graphite (the other diamond), one of the two purest forms of carbon. This form of carbon atoms arranged in a two-dimensional hexagonal structure provides not only a two-dimensional example of the material in nature, but also the extraordinary properties of graphene. With its mechanical, electrical, thermal and optical properties, graphene has revolutionized science in the last decade. Thanks to these features graphene is used in many fields such as transistors, battery technology, sensors, hydrogen storage, electronic devices, optical devices, water purification and biotechnology.

MATERIALS AND METHODS:

Graphene-containing 2-hydroxyethylcellulose (HEC) nanocomposite films, with or without drug (Doxorubicine), were prepared by solvent evaporation technique. We examined the film properties depending on the amount of graphene and HEC. We made structural, thermal and surface characterizations using FT-IR, TGA and SEM methods. The drug release was studied at two different pH values.

RESULTS:

The structure of DOXO loaded 2-HEC-graphene nanocomposite films was confirmed by DSC, XRD, FT-IR and elemental mapping methods. After 1 day, 60 % of DOXO was released at the acidic pH (pH = 4.5), while only 40 % of DOXO was released at the physiological pH of 7.4. The pH-dependent DOXO release of graphene-doped 2-HEC films is useful for treating tumor site with slightly acidic pH microenvironment.

CONCLUSIONS:

The presence of a graphene in the cellulosic structure contributes to the development of controlled drug release.

REFERENCES:

1. Depan D, Shah J, Misra RDK (2011). Materials Science and Engineering C, 31:1305–1312.
2. Tan JM, Karthivashan G, Arulselvan P, Fakurazi S, Hussein MZ (2014). Drug Design, Development and Therapy 8:2333–2343.
3. Manocha B, Margaritis A (2010). Journal of Nanomaterials Volume 2010, Article ID 780171.

P-357: PREPARATION OF POLY N-VINYLTRIAZOLE HYDROGELS HAVING ACID FUNCTIONALITIES FOR CONTROLLED DRUG RELEASE

Alemdar, S., Pekel Bayramgil, N.

Hacettepe University, Faculty of Science, Department of Chemistry, 06800, Beytepe, Ankara, Turkey

INTRODUCTION:

Hydrogels exhibit great similarities to living tissues because of their physical properties, such as their ability to absorb large amounts of water in their structures and their soft and flexible structures. Hydrogels are also used in controlled release technology in recent years due to their high biocompatibility. Tuberculosis remains an important health problem in our country and all over the world. Mycobacterium tuberculosis is the most common cause of death from single infectious agent-related deaths. 8 million new cases are reported annually and 2 million people die due to this disease. Today, the first drugs used in the treatment of tuberculosis are streptomycin, isoniazid, rifamycin, ethambutol and pyrazinamide. In this study, a series of polyvinyltriazole hydrogels containing vinylsulfonic acid, vinylphosphoric acid, itaconic acid group were investigated for the efficacy of rifamycin, a drug used in the treatment of tuberculosis.

MATERIALS AND METHODS:

Structural and thermal characterizations of hydrogels were examined using FTIR and TGA methods and rifamycin release using UV-vis spectrophotometer at 522 nm. The drug molecules are adsorbed onto the hydrogel structure. For this purpose, hydrogels were poured into the drug solutions prepared at pH = 7 and UV measurements were made with the part taken from the drug solution for a certain period of time. The drug release was studied at two different pH values and the release rates were calculated according to the amount of drug adsorbed per dry gel.

RESULTS:

In drug adsorption to hydrogels, it was observed that the most drug was held in hydrogels containing VSA and at least VPA. This result is explained by both swelling and acidity. According to the swelling curves, the water swelling ratio of hydrogel containing VSA is 65000%. However, as the acidity of sulfuric acid is higher than the other two, more rifamycin diffuses along with the water as a consequence of the high swelling. Rifamycin has 2 pKa since it is a Zwitterion, pKa 1.7 related to 4-hydroxy and pKa 7.9 related to 3-piperazine nitrogen. Therefore, it is also possible to say that the coupling of sulfuric acid groups via the basic piperazine group is carried out.

CONCLUSIONS:

Due to the chemical structure and the pKa values of the acid group added with polyvinyltriazole, it is concluded that it influences the drug release.

REFERENCES:

1. Kydoieus AF (1980). In: Kydonieus AF (ed). Controlled Release Technologies, Methods, Theory and Applications, Vol. I & II, CRC Press, Boca Raton.
2. Langer R (1980). Chemical Engineering Communications, 6:1.
3. Brannon Peppas L (1997). Medical Plastics and Biomaterials, 34.

P-358: STABILITY OF GEMCITABINE HYDROCHLORIDE LOADED LPHNS IN PHOSPHATE BUFFER SOLUTION AND FETAL BOVINE SERUM

Yalcin, TE., Ilbasmis Tamer S., Takka S.

Gazi University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Analysis of properties of nano-sized drug carrier systems in various physiological media is very important for in vivo applications. Serum proteins would alter the colloidal characteristics of nanocarriers such as particle size. The aim of this study was to evaluate colloidal stability of gemcitabine hydrochloride loaded LPHNs in various media.

MATERIALS AND METHODS:

To determine the colloidal stability of gemcitabine hydrochloride loaded LPHNs, lyophilized LPHNs were resuspended in different media (pH 7,4

phosphate buffer solution, fetal bovine serum (FBS) and phosphate buffer solution containing 10% FBS) and incubated at 37±1°C for 5 days (1). The mean particle size, polydispersity index and zeta potential were measured at predetermined time points to evaluate the stability of LPHNs.

RESULTS:

In pH 7,4 phosphate buffer solution media, the particle size of the LPHNs did not statistically change (p>0,05) for a period of 5 days. The LPHNs formulations had a size increase from 241 nm to 253 nm within 3 days of incubation in FBS 10% media (p>0,05), while

formulations had a significant size increase from 248 nm to 456 nm at the same incubation time in FBS 100% media (p<0,05). All formulations had negative zeta potential in all media.

CONCLUSIONS:

The particle size of LPHNs remained unchanged in all media at least 2 days. In FBS media (10% and 100%) the increase in particle size could be explained by the fusion of protein molecules on the surfaces of LPHNs. These results show that, LPHNs formulations can be stable for longer periods of time in blood.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-113S841)

REFERENCES:

1. Zhao J, Zhao M, Yu C, Zhang X, Liu J, Cheng X, Lee RJ, Sun F, Teng L, Li Y (2017). International Journal of Nanomedicine, 12:6735-6746.

P-359: STABILITY OF GEMCITABINE HYDROCHLORIDE LOADED LPHNS ON DIFFERENT STORAGE CONDITIONS

Yalcin, TE., Ilbasmis Tamer S., Takka S.

Gazi University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Liposomes and polymeric nanoparticles are two important classes of the nano-sized drug carrier systems. Recently, a new class of therapeutic nanocarriers known as lipid–polymer hybrid nanoparticles (LPHNs) have emerged as a promising drug delivery system to overcome the possible drawbacks and to integrate the positive attributes of liposomes and polymeric nanoparticles (1). The aim of this study was to investigate storage stability of gemcitabine hydrochloride loaded LPHNs.

MATERIALS AND METHODS:

A double emulsion solvent evaporation method was used to prepare gemcitabine hydrochloride loaded LPHNs (2). The stability of gemcitabine hydrochloride loaded LPHNs was monitored at 4°C, 25°C for 12 months and 40°C for 6 months. The mean particle size, polydispersity index, zeta potential, and retention rate of LPHNs were measured during the stability study. To characterize the surface morphology of the LPHNs, they were also imaged by transmission electron microscopy (TEM).

RESULTS:

At 4°C and 25°C, the particle size of gemcitabine hydrochloride loaded LPHNs showed physical stability for a period of 9 and 6 months, respectively (p>0,05). However, formulation showed stability for a storage period of 3 months at 40°C (p>0,05), by the end of 6 months, the particle size significantly increased from 216 to 336 nm with a high polydispersity index (0,648) at the same climatic condition.

CONCLUSIONS:

LPHNs were physically stable until 12 months at 4°C and 9 months at 25°C. When accelerated conditions are employed (40°C/75% RH), LPHNs lost the physical stability.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-113S841)

REFERENCES:

1. Zhang L, Zhu D, Dong X, Sun H, Song C, Wang C, Kong D (2015). International Journal of Nanomedicine, 10:2101-2114.
2. Mandal B, Bhattacharjee H, Mittal N, Sah H, Balabathula P, Thoma LA, Wood GC (2013). Nanomedicine, 9:474-91.

P-360: EFFECT OF VARIOUS FORMULATION PARAMETERS ON THE CHARACTERISTICS OF BLANK PLGA NANOPARTICLES

Copur, T., Bozdag Pehlivan, S., Öner,L.

Hacettepe University, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

The purpose of this study is to examine the effects of various formulation parameters on the physicochemical properties of PLGA nanoparticles.

MATERIALS AND METHODS:

PLGA nanoparticles were prepared by W/O/W multiple emulsion solvent evaporation method (1). Briefly, aqueous phase (inner) containing Polysorbate 80 was added to organic phase ((0.1%(w/v) PLGA in dichloromethane), then was emulsified by means of sonication for 3 min at 60 W (Bandelin Ultrasonic Probe). This emulsion was dispersed in the first outher phase including Polysorbat 80 and sonicated for 5 min at 60 W then was diluted in second outer phase and was stirred for 4 h at room temperature (Table 1). Nanoparticles washed, frozen at -80°C and lyophilized.

Table 1. Formulation parameters of PLGA nanoparticles.

Code	Volume of organic phase (mL)	Polysorbate amount in first / second outher phase (%)	Volume of first / second outher phase (mL)
F1	2.5	0.1 / 0.36	15 / 15
F2	3	0.1 / 0.36	15 / 15
F3	4	0.1 / 0.36	15 / 15
F4	2.5	0.3 / 0.36	15 / 15
F5	3	0.3 / 0.36	15 / 15
F6	4	0.3 / 0.36	15 / 15
F7	3	0.3 / 0.36	5 / 25
F8	3	0.3 / 0.36	7.5 / 22.5
F9	3	0.3 / 0.36	10 / 20

RESULTS:

Increase in the volume of organic phase caused increasing particle sizes of the F1 and F3 formulations, while no significant changes were measured in particle size values of the F4, F5 or F6 coded formulations. Also, increase in the volume of first outher phase caused the decreasing the particle size of the F7, F8 or F9 coded formulations. No significant changes were observed in zeta potential values prepared with different formulation parameters (from 37.5 mV to -31.2 mV).

CONCLUSIONS:

It can be concluded that formulation parameters such as volume of organic phase or volume of first outher phase have significant effect of the particle size of PLGA nanoparticles prepared.

REFERENCES:

1. Bozdag S, et al. (2005). Journal of Pharmacy and Pharmacology, 57 (6), 699-707.

P-361: THE EFFECT OF TYPE AND CONCENTRATION OF CHITOSAN ON THE ELECTROSPUN POLY(CAPROLACTON) NANOFIBERS

Eren Boncu, T., Ozdemir, N.

Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Poly(caprolactone)(PCL) and chitosan are polymers used in the production of controlled release formulations (1-3). The aim of the study is to produce PCL and PCL/chitosan nanofibers, which have attracted considerable interest in recent years due to the high tissue compatibility. In this study, electrospinning was used for the production of nanofibers. Furthermore the effects of the amount and type of chitosan on the fiber diameter and in vitro drug release from nanofibers were investigated.

Materials and Methods:. Polymers and glasial acetic acid (GAA) were purchased from Sigma-Aldrich. Nanofibers were producted by an electrospinning system (Ne-200, Inovenso/Turkey).10 % PCL or the mixture of 1-1,5 % v/w of chitosan/10 % v/w of PCL were dissolved in GAA, then active material (linezolid) was added to this solution. The solutions were poured in a plastic syringe. For electrospinning of the solution the voltage was applied at 15 kV with 1,5 ml/h flow rate and the distance between the needle and collector was fixed at 18 cm. The average diameters of fibers were calculated using ImageJ from SEM images. Static method was used for dissolution tests in 20 mL of PBS at 37°C (n=3).The results were used to fit to the different kinetics.

RESULTS:

Drug release was extended to10 days with PCL/ MMW chitosan formulations when compared with the PCL nanofiber. The changes in the concentration of chitosan did not cause a significant difference on the release of linezolid. The diameter of nanofibers was increased when chitosan was incorporated into the formulations.

CONCLUSIONS:

It can be stated that nanofibers were produced from PCL and PCL/chitosan. The release of active material from fibers can be modified by changing the molecular weight of chitosans.

REFERENCES:

1. Karuppuswamy P et al., (2015). Materials Letters, 141:180-186.
2. Zupančič Š et al., (2015). Journal of Drug Delivery Science and Technology, 30:408-416.
3. Roozbahani F et al., (2015). Journal of Nanomaterials, 1-11.

P-362: THE EFFECT OF GOLD NANOPARTICLES, SOLID LIPID NANOPARTICES AND GLYCOIN COMBINATIONS ON THE VIABILITY OF DERMAL FIBROBLASTS

[1] Payze, U., [2] Aydın Kose, F., [1] Gokce, EH.

[1] Ege University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Izmir, Turkey

[2] Ege University, Faculty of Pharmacy, Department of Biochemistry, Izmir, Turkey

INTRODUCTION:

Gold nanoparticles(AuNP) have been widely employed for biomedical applications and diagnostics, and have seen increasing use in the area of therapeutics (1). This study was undertaken to evaluate the effects of gold nanoparticles, vitaminE-loaded SLNs and glycoin combinations on NIH/3T3-cells for screening the right ratio of the formulation of a new product for lip care.

MATERIALS AND METHODS:

Cells were grown in conventional cell culture conditions and fed with DMEM medium containing 10%FBS at 37 ℃ as, in a 5%CO2 incubator.The intervals were controlled by phase contrast microscopy. AuNP, vitaminE-SLN, Glycoin and trehalose(as cryoprotectant) were examined by MTT cell viability assay in NIH/3T3-cells for 24-hours, separately and in combination (2).The formulation was produced by melting/fusion-method. AuNP, vitaminE-SLN, Glycoin and trehalose were added according to the data of cell culture studies. SLN was prepared by hot homogenization followed by high shear mixing.

RESULTS:

The size of SLN was 647.5nm±16.2;zeta potential was -27.8±2.71mV and polydispersity index was 0.4.Cell viabilities were examined for toxicity and IC50 value by using cell culture studies for Glycoin as first step. Formulation experiments containing Glycoin in different ratios were evaluated and the ideal was determined(2%).Formulation experiments with Trehalose-added-SLN at different ratios and SLN-without-vitaminE, vitaminE-SLN and vitaminE-alone were examined and the effect on the formulation was observed.The significant positive effects of vitaminE-SLN and 1%(w/v)trehalose on cell viability were determined.Formulation experiments containing AuNP were evaluated the ideal value was determined,keeping the 2%Glycoin content constant(AuNP0.0025%(w/w)).The final formulation, which was optimized by cell culture, was compared. The proliferation of the final formulation obtained was 227.2%.

CONCLUSIONS:

In this study, synergistic effect was observed by taking advantage of the natural and biocompatible ingredients of the formulation, which was proven by the cell culture.The proliferation effect was obtained by vitaminE- loaded SLNs as well as by the effect of the gold-nanoparticles and Glycoin.The ratio of the ingredients was screened by their effect on cell proliferation and the final formulation enhanced the viability up to 227.2%. According to the studies carried out gold-nanoparticles, vitaminE loaded SLNs and Glycoin is a promising formulation because of its unique structure in the field of lip care.

ACKNOWLEDGEMENTS:

This project was supported by Ege University Scientific Research Fund with a project number of 16/ECZ/021.

REFERENCES:

1. Yeh YC, et al. (2012) Nanoscale, 4(6):1871-80.
2. Re R, et al., (1999) Free Radic Biol Med, 26:7-1231.

P-363: PREPARATION AND IN VITRO CHARACTERIZATION OF CARVEDILOL LOADED POLYMERIC NANOPARTICLES FOR DRUG DELIVERY

[1] Guven, UM., [2] Ozturk AA., [2] Yenilmez E.

[1] Cukurova University, Department of Pharmaceutical Technology, Adana, Turkey

[2] Anadolu University, Department of Pharmaceutical Technology, Eskisehir, Turkey

INTRODUCTION:

Nanoparticles are one of the multiparticulate delivery systems and are prepared to improve bioavailability or stability (1). The object of the study was to formulate and characterize Eudragit® Nanoparticles containing carvedilol by determining their size and zeta potential, their external morphology for the treatment of hypertension.

MATERIALS AND METHODS:

Carvedilol loaded polymeric nanoparticles were prepared by Spray Dryer (Spray-Dryer B-90, BÜCHI, Switzerland) (2). The polymeric nanoparticles were characterized by a Zetasizer Nano ZS (Malvern Instruments, UK). The morphology of the nanoparticles were determined with a scanning electron microscopy. Interaction of drug with the polymers were determined by XRD and FT-IR.

RESULTS:

Particle size data showed submicron size with low polydispersity. The studies showed that carvedilol loaded particles have considerably high zeta potentials (Table 1). XRD and FT-IR analyses showed that neither active agent nor polymeric structure were affected from the production parameters.

Table 2: Particle size, zeta potential and PDI of carvedilol-loaded polymeric nanoparticles

Code	Particle Size (nm)	Polydispersity Index (PDI)	Zeta Potential (mV)
CL-P	418.2±18.5	0.4±0.02	40.1±1.1
CS-P	402.3±22.0	0.5±0.01	42.3±1.4
CSL-P	416.3±12.5	0.5±0.07	42.4±1.5
CL-1	535.5±13.8	0.4±0.07	41.2±.1.3
CS-1	529.4±10.2	0.5±0.06	40.6±2.4
CSL-1	530.4±10.4	0.6±0.02	40.6±2.3

CONCLUSIONS:

The carvedilol loaded polymeric nanoparticle systems developed in this study represent a promising safe system for the sustained and controlled delivery of carvedilol. The developed formulation is suitable, and represents a promising system for the sustained delivery of carvedilol to target cells, tissues and organs.

REFERENCES:

1. Kalimutu S, Yadav AV (2009). International Journal of PharmTech Research, 1(2): 179-183.
2. Sahoo J, Murthy PN, Biswal S (2009). AAPS Pharm Sci Tech, 10(1): 27-33.

P-364: IN VITRO RELEASE STUDIES AND HPLC METHOD FOR THE DETERMINATION OF CARVEDILOL IN NANOPARTICLE SYSTEMS

[1] Guven, UM., [2] Ozturk, AA., [2] Yenilmez, E.

[1] Cukurova University, Department of Pharmaceutical Technology, Adana, Turkey

[2] Anadolu University, Department of Pharmaceutical Technology, Eskişehir, Turkey

INTRODUCTION:

Nanoparticle systems are one of the multiparticulate delivery systems and are prepared to improve bioavailability or stability (1). Many advantages of nanoparticle-based drug delivery have been recognized. In vitro drug release studies are important and this studies help in evaluation of sustained and prolonged release dispersion systems (2). In this study, carvedilol loaded polymeric nanoparticles are determined of drug entrapment efficiency and characterized for in vitro release studies.

MATERIALS AND METHODS:

Entrapment efficiency was estimated by using the HPLC method. In vitro drug release of carvedilol from polymeric nanoparticles were studied through dialysis bag membrane. The temperature was maintained at 37 ± 0.5°C under sink conditions.

RESULTS:

The HPLC method developed was validated for precision, accuracy, specificity and linearity for carvedilol. HPLC conditions are shown in Table 1. Carvedilol loaded nanoparticle formulations were analyzed for entrapment efficiency by HPLC. The in vitro release studies indicated that, although there was an important burst release of the drug in 1 h, it continued in a sustained release way for 48 h.

Table 1. Chromatographic conditions

Stationary Phase	InertSustaine® column (4.6mmx150 mm, C18 Gravity, 3 µm)
Mobile Phase	0.03M potassium dihydrogen phosphate (pH 3.0) buffer: acetonitrile: methanol (60:50:10, v:v:v)
Oven Temperature	40 °C
Flow Rate	0.5 mL/min
İnjection Volume	20 µL
Detection Wavelenght	242 nm

CONCLUSIONS:

This developed HPLC method was also successfully applied for the determination of carvedilol in polymeric nanoparticle formulations, encapsulation efficiency and in vitro release study. The developed formulation is suitable, and represents a promising system for the sustained delivery of carvedilol.

ACKNOWLEDGEMENTS:

The authors would like to thank Santa-Farma (İstanbul, Turkey) for providing a gift sample of Carvedilol.

REFERENCES:

1. Kalimutu S, Yadav AV (2009). International Journal of PharmTech Research, 1(2): 179-183.
2. Venkateswarlu V, Manjunath K (2004). Journal of controlled release, 95(3): 627-638.

P-365: DEVELOPMENT AND IN VITRO / IN VIVO EVALUATION OF BISPHOSPHONATE LOADED MEMBRANES FOR GUIDED BONE REGENERATION

[1] Oz, UC., [1] Kucukturkmen B., [1] Saka,OM., [1] Devrim B., [2] Toptas, M., [3] Ozdemir, Ozge., [4] Bilgili, HM. [5] Deveci, S., [6] Unsal, E., [1] Bozkir, A.

[1]Ankara University Faculty of Pharmacy Department of Pharmaceutical Technology, Ankara, Turkey

[2]Bezmialem University Faculty of Dentistry Department of Periodontology, İstanbul, Turkey

[3]Cumhuriyet University Faculty of Veterinary Medicine Department of Surgery, Sivas, Turkey

4Ankara University Faculty of Veterinary Medicine Department of Surgery, Ankara, Turkey

5Health Sciences University Gulhane Medical Faculty Pathology and Cytology Department, Ankara, Turkey

6Ankara University Faculty of Dentistry Department of Periodontology, Ankara, Turkey

INTRODUCTION:

The aim of this research is utilization of membrane formulation as a barrier material for guided bone regeneration (GBR). The principal idea was developing a biodegradable barrier material preventing soft tissue migration through defect area during bone formation period and promoting osteoblast cells activity with minimized dose of Zoledronic Acid (ZA).

MATERIALS AND METHODS:

Membranes were prepared by polymer solution casting and evaporation. During the process, various amounts of PDLA, TEC, Pluronic F-127 and ZA were dissolved respectively in 5 mL of acetone and poured onto PTFE mold. Afterwards, solvent was evaporated at 37°C during 24 hours.

The morphology of membrane was observed using scanning electron microscopy (SEM) with acceleration voltage of 10kV.

The membranes were cut into 0.5 cm x 1 cm strips. Strain and tensile strength measurements were performed using a TA-XT plus texture analyser.

The in vitro release of zoledronic acid from membrane formulations was performed using the dialysis membrane method.

Efficacy of GBR membranes was investigated by implanting in 0.5x0.5 cm critical size defect in tibia and femur of New Zealand female rabbits. Histopathological analysis were performed to check bone healing.

RESULTS:

The SEM image of the membrane clearly demonstrated that the surface of membrane was essentially smooth. Testing of tensile strength was carried out to determine the effect of TEC on the mechanical properties of PDLA membranes. This test provides an indication of the ease of bending and shaping or cutting of the membranes when the periodontists or orthopedists need to apply them to the scar tissue. The tensile strength results revealed that, with increasing TEC content of membranes, higher tensile strength values were observed. Findings indicate the complete release of the water soluble drug (ZA) from the prepared membrane was achieved over a 6 h period. According to the histopathological results at the 8th week of the “control group” where any membrane application was performed, 70% of the defect area did not fill and only fibroblast formation (fibrosis) was observed in 30% of the defect area with very poor cartilage tissue formation. Fibrosis was observed on the surface of all periodic specimens, but no cartilage structure was observed. In ZA loaded membranes, woven bone formation was observed in the first 4 weeks, lesion and single bone formation were observed up to 6 weeks and complete healing was observed at the end of 8th week.

CONCLUSION:

Here in this report, we propose the utilization of bisphosphonate loaded biodegradable membrane formulations at GBR for the first time. Results suggests that local application of bisphosphonate loaded membrane formulations enhances bone formation compared to blank membranes and control group.

ACKNOWLEDGEMENTS:

This research is funded by Turkish Scientific and Technological Research Council (TÜBİTAK grant number 112S533).

P-366: MICROBIOLOGICAL AND EX VIVO PERMEATION/PENETRATION STUDIES OF VORICONAZOLE LOADED IN SITU GELS

[1] Ustundag Okur, N., [1] Yozgatli V., [2] Yoltas, A.

[1]Istanbul Medipol University, School of Pharmacy, Department of Pharmaceutical Technology, Istanbul, Turkey

[2]Ege University, Faculty of Science, Department of Biology, Fundamental and Industrial Microbiology Division, Izmir, Turkey

INTRODUCTION:

Fungal keratitis is a leading cause of serious ocular morbidity and blindness (1). Voriconazole (VCZ) is a potent new triazole derivative with a broad spectrum of antifungal activity against many fungal pathogens (Candida, Cryptococcus and Aspergillus species)(2). The aim of this study was to develop VCZ loaded ocular in situ gels and to evaluate microbiological activities and ex vivo permeation/penetration properties of these formulations.

MATERIALS AND METHODS:

In situ gel formulations were prepared by cold method (1) using poloxamer 188, poloxamer 407 (IS-1, IS-2, IS-3 and IS-4) and 0.3% carboxymethyl cellulose (IS-5, IS-6, IS-7 and IS-8). These formulations were evaluated for clarity, sol-gel transition temperature, gelling capacity, pH, viscosity and drug content. Sterility studies, determination of MIC of VCZ, disk diffusion testing were performed. C.albicans, C.tropicalis, A.fumigatus, A.niger, A.terreus and A.Flavus microorganisms were used for microbiological studies. IS-1 and IS-5 coded formulations were selected for ex vivo studies. Ex-vivo penetration/permeation studies were performed with rabbit cornea in diffusion cells.

RESULTS:

In situ gels were developed successfully and the characterization of the formulations has shown that formulations were suitable for the ophthalmic application. Formulations were detected to be sterile. MIC90 values of VCZ were determined as 0.25µg/ml for all of the microorganisms. According to disk diffusion test results, VCZ loaded formulations were found to be more effective on filamentous fungi than yeasts. The amount of VCZ permeated through cornea from IS-1 and IS-5 was determined approximately 38 – 39 % in the receptor compartment. The penetrated amount in the cornea was determined for IS-1 and IS-5 formulations 4.991±1.056% and 7.569±0.252%, respectively.

CONCLUSIONS:

According to obtained results, developed in situ gels are suitable for ocular drug delivery. VCZ loaded formulations were determined sterile and they

are effective to against C. albicans, C. tropicalis, A.fumigatus, A.niger, A.terreus and A.flavus which they may cause fungal keratitis. Ex vivo permeation/ penetration results also indicate that the formulations are suitable for the ocular drug delivery. So, in situ gelling systems could be offered a promising strategy for eye treatment.

REFERENCES:

1. Ustundag Okur N, Yoltas A, Yozgatli V (2016). Turk J Pharm Sci, 13:311–317.
2. Ustundag Okur N, Caglar ES, Yozgatli V (2016). Marmara Pharm. J., 20:79.

P-367: PREPARATION AND CHARACTERIZATION OF PLGA-LECITHIN NANOPARTICLES

Ozkan,Y., Esim, O., Savaser, A., Ozkan, CK., Tas.,C.

University of Health Sciences, Department of Pharmaceutical Technology, Ankara, Turkey

INTRODUCTION:

Lipid-polymer nanoparticles, which are made up of a polymer nanoparticle core and a lipid coat, present a more clinically feasible than liposomes and polymeric nanoparticles because they are physically robust as result of their polymer matrix cores , less toxic than polymeric nanoparticles and likely to possess penetrating abilities of liposomes, which are attributed to the phospholipid layers on the polymer nanoparticle surface (1).

MATERIALS AND METHODS:

To prepare PLGA-lecithin nanoparticles, 1 mL of Eletriptan Hydrobromide solution (3 mg/mL) water was emulsified using probe sonicator for 60 s at 30 W in 3 mL of DCM containing 90 mg of PLGA, 30 mg of PC, and 9 mg of TPGS to form the primary water/oil (w/o) emulsion. This emulsion is subsequently poured into 12 mL of deionized water and emulsified again for another 60 s at 30 W to form the water/oil/water (w/o/w) emulsion. The DCM was evaporated using rotary evaporator. The resulting nanoparticles were washed three times by centrifugation and re-suspension to remove any non-entrapped drug and excess PC. The encapsulation efficiency and drug loading were determined by HPLC. The volume-averaged sizes and the zeta potentials of the nanoparticles were measured. The nanoparticle morphologies were characterized by transmission electron microscopy.

RESULTS:

The nanoparticle size raised from 228.0±11.2 nm to 916.5 ± 23.8 nm when lechitin was added to the formulation, which shows the lechitin coating of nanoparticles. The TEM image of the loaded hybrid nanoparticles illustrates their spherical morphology.

CONCLUSIONS:

It can be concluded from the study that it is possible to prepare PLGA-lecithin nanoparticles. The effects of variations in surfactant were evaluated through changes in the size of the nanoparticles. As further studies, this nanoparticles can be used in various root of administration for drug delivery studies.

REFERENCES:

1. Cheow, Wean S, and Hadinoto, K Particuology 10.3 (2012): 327-333.

P-368: EXPERIMENTAL EVALUATION OF ANTINOCICEPTIVE ACTIVITY OF END-LAA LOADED POLYMERIC MICELLES WITH TAIL FLICK MODEL

[1] Sezgin Bayindir, Z., [1] Yuksel, N., [2] Kose Ozkan, C., [3] Savaser, A., [4] Varamini, P., [3,4] Toth, I.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

[2]Gulhane Education and Research Hospital, University of Health Sciences, Ankara, Turkey

[3]University of Health Sciences, Center of Pharmaceutical Sciences, Department of Pharmaceutical Technology, Ankara, Turkey

4The University of Queensland, School of Chemistry and Molecular Biosciences, and Centre for Integrated Preclinical Drug Development, Brisbane, Australia

5The University of Queensland, School of Pharmacy, Brisbane, Australia

INTRODUCTION:

Morphine-like analgesics are particularly effective in the treatment of neuropathic pain, but have serious side effects. As an alternative, it has been shown that Endomorphin-1 is more effective in the treatment of neuropathic pain and the side effects are less due its endogenous nature (1). However End-1 is not clinically used due to its instability and inability of crossing the Brain-Blood-Barrier. A lipid-modified derivate of Endomorphine-1 peptide (End-LAA) was previously synthesized and loaded in polymeric micelles to overcome these problems and improve in vivo performance of the drug (2). The aim of current study is to test the efficiency of End-LAA loaded polymeric micelles with in vivo experiments and compare the outcomes with pure Endomorphine-1.

MATERIALS AND METHODS:

End-LAA was loaded into Pluronic F127 micelles by film formation method as previously reported (2). A thermally stimulated tail flick test device sensitive to opioids (Columbus, OH, USA; Type 812) was used in evaluating the efficacy of drugs in acute pain. The tail flick test was performed on Wistar rats upon oral and intravenous administration of End-LAA, Endonorphine 1 and micellar formulation. Tail flick times at 1, 1.5, 2, and 3 hours after 15, 30, and 45

minutes after oral administration and 1, 1.5, 2, and 3 hours after 10, 20, and 30 minutes after intravenous administration were measured and the percentages of maximum possible effect (% MPE) were calculated. The increase in tail flick time compared to baseline values was considered an analgesic effect.

RESULTS:

Intravenously administered micelle formulation significantly extended the tail flick time in rats compared to pure End-LAA, Endo-1 and control groups. Pure End-LAA prolonged the tail flick time of rats significantly after oral administration compared to Endo-1 and control groups.

CONCLUSIONS:

Overall study revealed that, upon intravenous administration micelle formulation increased the analgesic effect in acute pain. This is thought to be due to the fact that polymeric micelles can prolong the drug circulation time in blood. Besides oral End-LAA was found to be effective as an oral analgesic for acute pain.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-115S834)

REFERENCES:

1. Fichna J, Janecka A, Costentin J, Do Rego JC (2007). Pharmacological Reviews, 59(1):88-123.
2. Sezgin Bayindir Z, Yuksel N, Varamini P, Toth I (2016). Arhiv Za Farmaciju Special issue, 319-320.

P-369: EFFECTS OF ANTIHYPERGLYCEMIC AGENTS ON QT INTERVAL VALUE OF DIABETIC RATS

[1] Yalin, AE., [2] Comelekoglu, U., [2] Ozbay, E., [1] Yildirim, M., [3] Berkoz, M.,[1] Yalin, S.

[1]Mersin University, Faculty of Pharmacy, Department of Biochemistry, Mersin, Turkey

[2]Mersin University, Faculty of Medicine, Department of Biophysics, Mersin, Turkey

[3]Yuzuncuyil University, Faculty of Pharmacy, Department of Biochemistry, Van, Turkey

INTRODUCTION:

Diabetes is a metabolic disorder characterized by increased blood glucose resulting from changes in carbohydrate, protein and lipid metabolism. These changes are likely to lead to the development of cardiovascular diseases(1). Prolonged QT may be a potentially sensitive marker of increased risk of cardiac arrhythmias and sudden cardiac death. Exenatide, sitagliptin and insulin are effective antihyperglycemic agents used in the treatment of diabetes(2). In this study, we aim to evaluate the effects of exenatide, sitagliptin and insulin on QT interval of diabetic rats.

MATERIALS AND METHODS:

Male Wistar rats were divided in five groups: control (C), diabetics (D; single dose 43 mg/kg streptozotocin), diabetic treated with exenatide (D+E; exenatide; single dose 43 mg/kg streptozotocin and 0.1 µg/kg exenatide per day for 15 days), diabetic treated with sitagliptin (D+S; single dose 43 mg/kg streptozotocin and 10 mg/kg sitagliptin per day for 15 days) and diabetic treated with insülin (D+I; single dose 43 mg/kg streptozotocin and 3 IU insuline per day for 15 days). Electrocardiography was recorded using Ag/AgCl electrodes. QT intervals were measured from this recordings.

RESULTS:

Rats of the D+I group presented significant prolonged QT interval ($p<0.05$), whereas rats of the D+S and D+E groups presented less prolonged intervals ($p>0.05$) than C and D rats. These prolongations were by 2.9% in group D, 11.7% in group D+E, 16.1% in group D+S and 33.3% in group D+I.

CONCLUSIONS:

Our findings have demonstrated that insulin treatment in diabetes causes the prolongation of QT interval, which is associated with ventricular arrhythmias and sudden death. This cardiovascular risk was less in rats of D+S and D+E groups. Further studies are needed to determine the mechanisms of QT interval prolongation induced by antihyperglycemic agents.

ACKNOWLEDGEMENTS:

This study was supported by Mersin University (Project No: 2017-2-AP3-2532)

REFERENCES:

1. Kannel WB (1985). Am Heart J 110:1100–1107
2. Kolterman et al., (2005). Am. J Health Syst Pharm. 62:173–181.

P-370: MODULATION OF HCT 116 P53 -/- CELL VIABILITY BY COENZYME Q0

Yaprak, A , Karabay, AZ

Ankara University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey

INTRODUCTION:

Colorectal cancer (CRC), also known as bowel cancer, develops in the colon and/or the rectum (the last several inches of the large intestine before the anus) (1). As reported by Turkish Ministry of Health, colon cancer is one of the five most common cancer types in Turkey (2). Coenzyme Q0 (CoQ0; 2,3-dimethoxy-5-methyl-1,4-benzoquinone) is a unique type of ubiquinone which mainly accumulates in mitochondria (3). It has been shown that different types of ubiquinones inhibit the opening of the pores such as PTP (permeability transition pore) which plays a significant role in mitochondrial transition,

maintains cellular redox balance and have strong antioxidant properties (4). In addition, studies have shown that types of Coenzyme Q0 have therapeutic effects for cancer, inflammation and metabolic disorders, and studies have reported apoptotic activity for Coenzyme Q0 in various cancer types (5,6). The effects of Coenzyme Q0 on colon cancer cells are largely unknown and therefore in this study we aimed to investigate the modulation of colon cancer cell viability by Coenzyme Q0.

MATERIALS AND METHODS:

HCT116 p53-/- colon cancer cells were seeded to 96 well plates and incubated with different concentrations of Coenzyme Q0 (0.5 uM-200 uM) for 24, 48 and 72 hours and then 20 ul of MTT solution (5 mg/ml) was added to cells for incubation. After 4 hours of incubation, formazan crystals were dissolved before measuring absorbance at 550 nm. Absorbance of cells treated without Coenzyme Q0 was served as control and the cell viability of Coenzyme Q0 treated cells was given as percentage of control group. Coenzyme Q0 treated and untreated cells were also collected and lysed for western blotting to detect PARP fragmentation.

RESULTS:

Coenzyme Q0 inhibited HCT 116 p53-/- cell viability at 25 uM and higher concentrations significantly ($p<0.05$) at 24, 48 and 72 hours of incubation periods. Coenzyme Q0 also induced apoptotic PARP fragmentation in HCT 116 p53 -/- cells.

CONCLUSIONS:

According to the results, Coenzyme Q0 decreases cell viability at certain doses. In conclusion, we showed that Coenzyme Q0 modulated cell viability in HCT 116 p53 -/- colon cancer cells. Further work is needed to clarify the biological mechanisms mediating these effects.

REFERENCES:

1. Donaldson, MS (2004). Nutrition journal 3(1): 19.
2. http://kanser.gov.tr/kanser/kanser-turleri/45-kalin-bagirsak-kanseri.html
3. Quinzii CM, Hirano M (2010). Developmental disabilities research reviews 16(2): 183-188.
4. Devun et al., (2010). PloS one 5(7): e11792.

P371: CYTOTOXIC EFFECTS OF SILICON PHTHALOCYANINE, NAPHTHALOCYANINE AND THEIR WATER SOLUBLE DERIVATIVES

[1] Ozel, A., [1] Barut, B., [2] Biyiklioglu, Z.

[1] Karadeniz Technical University, Faculty of Pharmacy, Department of Biochemistry, Trabzon, Turkey

[2] Karadeniz Technical University, Faculty of Science, Department of Chemistry, Trabzon, Turkey

INTRODUCTION:

Cancer, one of the major health problems, is the second leading cause of death in worldwide (1). Despite the most common modalities for cancer are surgery, chemotherapy and radiotherapy, they have serious side effects such as cardiotoxicity, neurologic disorders. Thus, scientists continue to seek for discovery and development of novel effective anticancer agents. Phthalocyanines, significant class of macrocyclic compounds, have biological and pharmacological properties including anticancer, antioxidant, antimicrobial, photodynamic therapy, topoisomerase inhibition (2, 3). In this research, silicon phthalocyanine, naphthalocyanine (1-2) and their water soluble derivatives (1a, 2a) were investigated against lung (A549), breast (BT-20), liver (SNU-398), prostate (DU-145), and melanoma (SK-Mel 128) carcinoma cell lines.

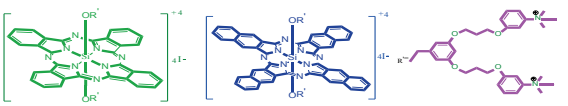


Figure 1. Water soluble silicon phthalocyanine and naphthalocyanine

MATERIALS AND METHODS:

The silicon phthalocyanine, naphthalocyanine and their water soluble derivatives were synthesized and characterized on previous studies. In this study, the cytotoxic activities of the compounds were determined against A549, BT-20, SNU-398, DU-145 and SK-Mel 128 carcinoma cell lines using MTT assay. Cisplatin was used as positive control.

RESULTS:

The Cell Cytotoxicity50 (CC50) values of the compounds (1-2a) were determined for five carcinoma cell lines. Compound 1a showed higher cytotoxic activities than among other tested compounds for all of five carcinoma cell lines. The CC50 values of the compound 1a were 2.24, 3.96, 0.86, 4.63 and 1.47 μM against A549, BT-20, SNU-398, DU-145 and SK-Mel 128 carcinoma cell lines whereas cisplatin CC50 values were 9.66, 21.99, 4.33, 1.66 and 13.99 μM against carcinoma cell lines. In addition compound 2a displayed higher cytotoxic properties with 11.85 μM than cisplatin against SK-Mel 128 carcinoma cell line. Compounds 1 and 2 had low and similar cytotoxic effect on A549 cell lines with CC50 values of 47.48 and 47.51 μM.

CONCLUSIONS:

Our studies results showed that compound 1a had considerable anticancer activities compare to positive control against all of five carcinoma cell lines. Thus, compound 1a is potential compound to be further developed as novel anticancer agent.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (116Z364).

REFERENCES:

1. Dünya Sağlık Örgütü- Kanser http://www.who.int/cancer/en/ Son erişim tarihi 18.04.2018.
2. Kantar C, Akal H, Kaya B, Islamoğlu F, Türk M, Şaşmaz S (2015). Journal of Organometallic Chemistry, 783: 28-39.
3. Shua L, Wang S, Zhang L, Fu B, Zhou X (2009). Chemistry & Biodiversity, 6:827-837.

P372: COMPARISON OF THE CYTOTOXIC EFFECTS OF DIFFERENT SOLVENTS ON HCT 116, HL-60 AND K562 CELL PROLIFERATIONS

Koc, A., Karabay, AZ., Buyukbingol, Z., Aktan, F.

Ankara University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey

INTRODUCTION:

To test the effects of some chemical, biologic, synthetetic or herbal products on cell culture models, the first step is testing their solubulity in organic solvents (1). It is very important that the selected organic solvents don't exhibit any toxic effects to the cells (2). In this study, we aimed to find out the toxicity induced by different solvents (ethanol, methanol, acetone, kloroform, hexane, ethyl acetate, DMSO) to three different cancer cell lines.

MATERIALS AND METHODS:

Human chronic myelogenous leukemia cell line (K562), colorectal cancer cell line (HCT 116), acute promyelocytic leukemia cell line (HL-60) were treated with different solvents (ethanol, methanol, acetone, kloroform, hexane, ethyl acetate, DMSO) at %0.5-%10 concentration range for 24, 48 and 72 hours. After incubation times, MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide) test was performed.

RESULTS:

We found that all tested solvents had differently effected the proliferation of HCT 116, K562 and HL-60 cells. When the cells were incubated with DMSO, ethyl acetate, acetone, methanol, ethanol, hexane and chloroform for 24, 48 and 72 h, all solvents decreased cell viability significantly ($p < 0.05$) at different concentrations in K562, HCT 116 and HL-60 cell lines.

CONCLUSIONS:

Since the solvents used in this study are widely used to dissolve different compounds and drugs for the treatment of cells, detailed information about their toxicity is valuable. In this study, we contributed to the literature with novel toxicity data of the solvents in different cell lines. Further research may reveal the underlying mechanisms of diminished cell viability induced by these different solvents.

REFERENCES:

1. Jamalzadeh et al., (2016). J Med Biochem.4(1): e33453.
2. Zapor et al., (2002). International Journal of Occupational Safety and Ergonomisc. 8(1): 121-129.

P-373: HYPERFERRITINEMIA AND INFLAMMATION IN METABOLIC SYNDROME PATIENTS DIAGNOSED WITH OR WITHOUT DIABETES

[1] Aca, HT., [2] Baba B., [3] Kirac CO., [4] Ozturk B., [2] Hacisevki A.

[1]KTO Karatay University, Health Sciences College, Department of Nutrition and Dietetics Konya, Turkey

[2]Gazi University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey

[3]Selcuk University, School of Medicine, Department of Internal Medicine, Division of Endocrinology and Metabolism, Konya, Turkey

4Selcuk University, School of Medicine, Department of Medical Biochemistry, Konya, Turkey

INTRODUCTION:

The metabolic syndrome (MetS) is a global public-health problem worldwide with the increasing prevalence. MetS is characterized by a cluster of risk factors, including insulin resistance (IR), dyslipidemia, central adiposity and elevated blood pressure that increase risk for cardiovascular disease, type 2 diabetes (T2DM) and all cause mortality (1-3). Inflammation is involved in insulin resistance, adiposity and other aspects of metabolic syndrome. Ferritin, acute phase reactant, has also been related to insulin resistance, MetS and diabetes. However, the association between increased serum ferritin levels and the metabolic syndrome still remains controversial (4,5). This study aimed at assessing whether ferritin and proinflammatory cytokine IFN-γ are associated with MetS patients with or without DM.

MATERIAL AND METHOD:

A total of 50 MetS patients and 30 controls without MetS were included in the analysis. The study group of MetS patients were divided into two subgroups according to have DM: the first MetS group who had DM included 26 subjects with the mean aged 52.73±1.4 years and mean BMI 36.7±1.5, the second group who had no DM included 24 subjects with the mean aged 34.7±2.1 years and mean BMI 32±1.1. The control group who had no DM included 30 subjects with the mean age 28.6±1.6 years and mean BMI 29.6±0.8. Serum ferritin and IFN-γ levels were determined by elisa kits. In addition, demographic data, body mass index, antrophometric measurements and biochemical parameters were evaluated.

RESULTS:

The levels of ferritin and IFN-γ of total patients were found significantly higher compared to controls ($p<0.05$). Significant differences were observed among serum insulin, glucose, total cholesterol, HDL-cholesterol, triglycerides levels, BMI, systolic and diastolic blood pressure, HOMA-IR, waist circumference in total patients compared to controls ($p<0.05$). There was no significant difference between subgroups according to ferritin and IFN-γ levels. The levels of ferritin of patients subgroups were found significantly higher compared to controls. Compared to controls, IFN-γ levels were found significantly higher in second group ($p<0.05$). Significant differences were determined among serum glucose, total cholesterol, waist circumference, HOMA-IR and BMI between subgroups ($p<0.05$).

CONCLUSIONS:

Our findings suggested that hyperferritinemia and inflammation may occur in MetS patients. Additional studies in larger groups are needed to confirm association of these parameters with the MetS.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Gazi University Research Foundation (02/2017-17).

REFERENCES:

1. Kaur J (2014). Cardiol Res Pract, 2014:943162.
2. Marsland et al., (2010). Metabolism, 59(12):1801-8.
3. Kang et al., (2012). Clin Chim Acta, 413(5-6):636-41.
4. González et al., (2006). Eur J Clin Nutr, 60(6):802-9.
5. Jin et al., (2015). Int J Clin Exp Med, 8(8):13317-22.

P-374: PHENYLBUTYRIC ACID MAY BE PHARMACOLOGICAL AGENT TO OBESITY ASSOCIATED INFLAMMATION

[1] Baba, B., [2] Caliskan, M., [2] Boyuk, G., [1] Hacısevki, A.

[1] Gazi University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey

[2] Ankara Yıldırım Beyazıt Training and Research Hospital, Ankara, Turkey

INTRODUCTION:

Obesity is a growing widespread epidemic with an alarming high prevalence (1, 2) and is closely associated with an increased risk for the development of metabolic diseases such as insulin resistance, type 2 diabetes mellitus, hypertension, hyperlipidemia, atherosclerosis, metabolic syndrome and cardiovascular disease (3). Obesity, which is defined as abnormal or excessive fat accumulation in adipose tissues, is a chronic inflammation disease (4). Adipose tissue is a complex organ that comprises a wide range of cell types with diverse functions. It contains various immune cells, the adipose tissue is now considered as an immune organ, at the cross-road between metabolism and immunity (2). A major player in systemic low-grade chronic inflammation in obesity is the increased numbers of adipose tissue proinflammatory macrophages and deregulated production and function of cytokines (5). The purpose of this study was to examine changes in inflammatory cytokines and the effect of chemical chaperon phenylbutyric acid on cytokine levels in ob/ob mice.

MATERIALS AND METHODS:

Twelve wild-type (lean) controls and ob/ob mice were recruited to the study. Oral vehicle or chemical chaperon administrations performed to lean and ob/ob mice for 1 month. Observed blood glucose concentrations at the fed state and body weights were evaluated in all mice. Blood samples collected at day 30. Plasma IL-10 and IL-12 levels were determined by using elisa kits.

RESULTS:

It was found that antiinflammatory cytokine IL-10 levels were increased and proinflammatory cytokine IL-12 levels were reduced in chaperon-treated ob/ob mice compared to ob/ob controls ($p<0.05$). Ob/ob controls demonstrated higher IL-12 levels compared to lean mice ($p<0.05$). However, there was no significant difference in terms of IL-10 levels in lean mice compared to ob/ob controls. When chaperon-treated ob/ob and lean mice compared, there was no significant difference in cytokine levels of groups. We found that IL-10 levels were higher and IL-12 levels were lower in chaperon-treated ob/ob mice compared to vehicle-treated lean mice ($p<0.05$). Blood glucose concentrations at the fed state in ob/ob controls were significantly higher compared to other groups.

According to body weights, there were significant differences between lean mice and ob/ob mice.

CONCLUSIONS:

Our results demonstrated that obesity is associated with inflammation and chemical chaperon administration ameliorate inflammation. Phenylbutyric acid may be a pharmacological agent to obesity associated inflammation but further investigation still requires to confirm these findings.

REFERENCES

1. Pahlavani et al., (2017). J Investig Med, 65(7):1021-1027.
2. Makki et al., (2013). ISRN Inflamm, 2013(139239):1-12.
3. Matia-García et al., (2016). Int J Clin Exp Med, 9(8):16596-16604.
4. Kawasaki et al., (2012). Scientific Reports, 2(799):1-7.
5. Castoldi et al., (2016). Front Immunol, 6(637):1-11.

P-375: HSP70 INHIBITOR MKT-077 ENHANCES THE ANTICANCER EFFECT OF PACLITAXEL IN MDA-MB-231 CELL LINES.

[1] Erdas, B., [2] Ergul, M.

[1]Cumhuriyet University, Faculty of Pharmacy, Sivas, Turkey

[2]Cumhuriyet University, Department of Biochemistry, Sivas, Turkey

INTRODUCTION:

Heat shock protein 70 (Hsp70) is a chaperone has several physiological roles, such as folding of nascent proteins, refolding of misfolded proteins, inhibition of protein aggregation, and involvement in intracellular protein transport (1). Hsp70 is marginally expressed in normal cells, but is excessively expressed in many types of cancer cells, helping cancer cells to survive in hard conditions (2). This protein plays important roles in many processes related to poor prognosis, including resistance to chemotherapy, inhibition of apoptosis, metastasis, and invasion. Therefore, specific inhibition of Hsp70 in cancer cells is a significant strategy in the treatment of cancer (3). The present study aimed to determine whether MKT-077 can enhance chemosensitivity to paclitaxel; for this purpose the combined effects of MKT-077 with paclitaxel on MDA-MB-231 cells were investigated.

MATERIALS AND METHODS:

Human breast adenocarcinoma MDA-MB-231 cells were cultured and treated with serial concentrations (100-10-1-0,1 μM) of MKT-077 alone or in combination with paclitaxel for 24 h. Antiproliferative activity of MKT-077, paclitaxel and combination treatment were evaluated using the XTT colorimetric assay.

RESULTS:

Our results revealed that the combination treatment synergistically inhibited cell proliferation in a dose-dependent manner. The IC50 values were calculated as 9,73 μM, 2,13 μM and 1,01 μM for MKT-077, paclitaxel and MKT-077-paclitaxel combination respectively.

CONCLUSIONS:

In conclusion, our findings showed that MKT-077 increased the antiproliferative effect of paclitaxel. This result suggests that MKT-077 in combination with paclitaxel may serve as a potentially useful therapeutic strategy for breast cancer patients.

Acknowledgements:

This study was supported by the Cumhuriyet Universtiy BAP (Project No: Ecz-045).

REFERENCES:

1. Radons J (2016). Cell Stress Chaperones. 21:379-404.
2. Leu JI, Pimkina J, Frank A, Murphy ME, George DL (2009). Mol Cell., 36:15-27.
   3. Rodina A, Patel PD, Kang, Y et all (2013). Chem Biol., 12:1469-1480.

P-376: USNIC ACID INHIBITS PROLIFERATION AND THE PROFILES OF EXPRESSION OF APOPTOSIS-RELATED GENES IN BREAST CANCER CELLS

Cansaran Duman, D.

Ankara University, Biotechnology Institute, Central Lab., Ankara, Turkey

INTRODUCTION:

Lichens produces a variety of secondary metabolites, many of which are unique to lichen symbioses (1). There has been an ever growing interest in pharmaceutical studies with many medicinally important organisms having been investigated as potential sources for new drug candidate molecules (2, 3). Usnic acid (UA), one of the most important secondary metabolites in lichens, is known to have many biological activities. The aim of this study was to investigate the effects of UA on proliferation and the changes of gene expression profile in breast cancer cells, MCF-7, BT-474, MDA-MB-431 and SKBR-3 and non-cancerous breast cell line MCF-12A.

MATERIALS AND METHODS:

Cell viability of UA treatment was assessed by MTT assay. Differential expression of apoptosis related 88 genes in breast cancer was determined by real-time PCR using the Human Apoptosis Primer Library qRT-PCR Array.

RESULTS:

Examined breast cancer cells were treated with UA (100, 50, 35, 25, 15, 12.5, 6.25, 3.125, and 1.562 μM) for 24, 48 and 72 h. UA exhibited time and dose dependence in all cell lines. UA showed almost no toxic effect on non-cancerous breast epithelial cell in this study. Thus its antiproliferative effects on cancer cells and less toxicity towards non-cancerous breast cells offers UA. MCF-7 cells were more sensitive to UA than other examined breast cancer cell lines (MDA-MB-231, BT-474, SK-BR-3). IC50 for UA in MCF-7, BT-474, MDA-MB-431 and SKBR-3 cells were 13.11, 12.65, 12.84, and 27.2 μM at 48 h, respectively. The cells were treated with IC50 values of the UA for apoptosis primer library array. Treatment of MCF-7 cells with UA (IC50=13.11 μM) for 48 h resulted in significant differential expression of 34 apoptosis related genes in breast cancer.

CONCLUSIONS:

In this study demonstrate that UA inhibits cell proliferation and alters expression of apoptosis related genes in breast cancer cells. This is the first report on full screen of apoptosis-related gene expression after treatment of UA. As a result of this study, UA may be a potential therapeutic agent for the treatment of breast cancer.

ACKNOWLEDGEMENTS:

We thank Ankara University, Management of Scientific Research Projects (Project no. 16H0415002 and 15B0415001), for the financial support.

REFERENCES:

1. Backorova M, Jendzelovsky R, Kello M, Backor M, Mikes J. Fedorocko P (2012). Toxicol in Vitro, 26(3):462-468.
2. Brisdelli F, Perilli M, Sellitri D, Piovano M (2013). Phytother Res, 27:431-437. 3. Shrestha G, St. Clair LL (2013). Phytochemistry Reviews, 12(1):229–244.

P-377: LEUKOTRIENE D4 LEVELS IN PATIENTS WITH BREAST CANCER

[1] Miser Salihoglu, E., [1] Akbas, KK., [2] Karanlik, H., [3] Demokan, S., [1] Yardim-Akaydin, S.

1 Gazi University, Faculty of Pharmacy, Department of Biochemistry Ankara, Turkey
2 Istanbul University, Institute of Oncology, Department of Surgery Istanbul, Turkey
[3] Istanbul University, Oncology Institute, Department of Basic Oncology Istanbul, Turkey

INTRODUCTION:

High expression of cysteinyl leukotriene D4 receptor, CysLT1R, is associated with a poor prognosis in several human cancers. Also, LTD4 was found to induce proliferation and survival in cancer patients. Here, we have determined serum leukotriene D4 (LTD4) levels in patients with breast cancer and examined its relationships with various parameters, including age, grade, menopausal status.

MATERIALS AND METHODS:

For that purpose, serum samples were taken from 58 patients diagnosed with breast cancer and 8 healthy controls. The patients were divided into five subgroups, as Luminal A, Luminal B, HER (+), Luminal B-HER (+) and triple negative. Leukotriene D4 levels were measured by ELISA method.

RESULTS:

Mean levels of LTD4 in the patients were significantly higher when compared with healthy controls [3,43 (2,21) ng/mL vs 1,47 (0,46) ng/mL; $p < 0.05$]. According to the molecular subtypes, serum LTD4 levels were found to be significantly higher in the Luminal B and Triple (-) subgroups than the controls ($p < 0,05$). Post-menopausal patients had higher levels of LTD4 than premenopausal patients ($p < 0,05$).

CONCLUSIONS:

Our study supports other studies showing the role of leukotrienes in cancer. Because of LTD4's ability to induce proliferation and inhibit apoptosis, increased levels of LTD4 in our study may be associated with cancer development, especially in post-menopausal women.

ACKNOWLEDGEMENTS:

This study was supported by a grant of GUBAP (02/2017-02)

REFERENCES:

1. Magnusson et al., (2007). Cancer Res. 67, 9190–9198.
2. Wang D, DuBois RN (2010). Nature Reviews Cancer, 10:181–193.

P-378: MRNA AND PROTEIN EXPRESSION LEVELS OF P53 IN MOLECULAR SUBTYPES OF BREAST CANCER

[1] Miser Salihoglu, E., [2] Demokan, S., [3] Karanlik, H., [4] Karahalil, B., [1] Yardim-Akaydin, S.,

1 Gazi University, Faculty of Pharmacy, Department of Biochemistry Ankara, Turkey
[2] Istanbul University, Oncology Institute, Department of Basic Oncology Istanbul, Turkey

[3] Istanbul University, Institute of Oncology, Department of Surgery Istanbul, Turkey

[4] Gazi University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Ankara, Turkey

INTRODUCTION:

p53 plays a role in restraining DNA exchange between imperfectly homologous sequences and thereby in suppressing tumorigenic genome rearrangements. Cells missing p53 can accumulate chromosomal

abnormalities because of the absence of p53-mediated cell-cycle arrest after double-stranded DNA breaks (1). The absence of p53 is a major predictor of poor response to classic chemotherapeutic agents (2). The objective of this study was to evaluate the expression of p53 gene and protein.

MATERIALS AND METHODS:

Real-time polymerase chain reaction (RT-PCR) test and Western blot were used to detect the expression of p53 in 24 breast cancer patients who have already been diagnosed with breast cancer due to their illness during surgery and 4 healthy women who haven't got any benign or malign histories and admitted to macromastia and breast reduction surgery as already decided by doctors.

RESULTS:

According to our data, tumor tissue p53 mRNA expressions were higher in 58% of patients than in normal tissues. Mean mRNA expression levels of p53 were higher, but not statistically significant, in tumor tissues than those in normal tissues of the same patients ($p>0.05$). Conversely, p53 protein levels were higher in normal tissues than in tumor tissues. There were positive correlations between normal and tumor tissue mRNA expressions and negative correlations between normal and tumor tissue protein expressions.

CONCLUSIONS:

Because p53 plays a role in DNA repair, decreased expression of p53 protein may be part of cancer development due to DNA damage. In contrast to p53 mRNA expression, decreased tumor tissue protein expression can reduce patients' response to chemotherapeutic agents.

ACKNOWLEDGEMENTS:

This study was supported by a grant of GUBAP (02/2017-01)

REFERENCES:

1. Akyuz et al., (2002). Molecular and Cellular Biology, 22(17):6306-6317.
2. Niederhuber et al., (2013). Abeloff's Clinical Oncology, 62.

P-379: SYNTHESIS AND APPLICATION OF NOVEL ACETYLCHOLINESTERASE INHIBITORS.

Doganer, M., Ozkan Hasanoglu, E., Sari, N., Arslan, F.

Gazi University, Faculty of Science, Department of Chemistry, Teknikokullar, Ankara, Turkey

INTRODUCTION:

Inhibition of acetylcholinesterase (AChE), the key enzyme in the breakdown of acetylcholine, is considered as a promising strategy for the treatment of neurological disorders such as Alzheimer's disease, senile dementia, ataxia and myasthenia gravis. Alzheimer's Disease(AD) is a chronic neurodegenerative disease which characterized by memory loss, difficulty in speaking, problems with communication and reasoning (1). There are many causes about the emergence of this disease, like genetic factors, autoimmune reactions and protein plaques (2). One of these reasons is cholinergic hypothesis that AD is caused by reduced synthesis of the neurotansmitter acetylcholine(ACh).One of these reasons is cholinergic hypothesis that AD is caused by reduced synthesis of the neurotansmitter acetylcholine(ACh). AChE inhibitors inhibit the hydrolysis reaction of ACh, so low ACh level at AD patients is raised (2,3). Many inhibitors such as tacrine, donepezil, physostigmine are used as drugs for AD treatment (3). In current study, we report synthesis, characterization and AChE inhibition properties of novel Schiff bases of based on 3,3'-(piperazine-1,4-diyl)bis(propan-1-amine).

MATERIALS AND METHODS:

Ligand of based on piperazine and its' Pt(II) complex were synthesized with 5-fluoro-3-methyl-salicylaldehyde. Inhibitors were characterized by elemental analysis, TGA, FT-IR, 1H-NMR, 13C-NMR spectroscopy. AChE activity of the synthesized compounds were investigated by spectrophotometric Ellman method (4). Inhibitors' IC50 values were determined.

RESULTS:

Synthesized inhibitors' elemental analysis, TGA, FT-IR, 1H-NMR, 13C-NMR spectroscopy results were observed at the expected values. As a result of spectrophotometric studies, it was seen that all compounds had reversible AChE inhibitor property. Piperazine-based Pt(II) complex showed a higher inhibition compared to the ligand. For the studied complexes all IC50 against AChE were in the micromolar range.

CONCLUSIONS:

In summary, new ligand of based on piperazine and its' Pt(II) complex were prepared. The structural characterizations of synthesized compounds were

made by using different spectroscopic methods. Novel Schiff bases of based on 3,3'-(piperazine-1,4-diyl)bis(propan-1-amine) have been prepared for preliminary screening as inhibitors against AChE. All the synthesized compounds behaved as inhibitors against AChE.

REFERENCES:

1. Akhondzadeh S, Noroozian M, Mohammadi M, Ohadinia S, Jamshidi AH, Khani M (2003). J Clin Pharm Ther., 28.
2. Rizzo S, Riviere C, Piazzi L, Bisi A, Gobbi S, Bartolini M, Andrisano V, Morroni F, Tarozzi A, Monti JP, Rampa A (2008). J Med Chem., 5:2883-2886.
3. Francis PT, Palmer AM, Snape M, Wilcock GK (1999).J Neurol Neurosur Ps., 66:137-147.
4. Ellman GL, Courtney KD, Andres V, Featherstone RM (1961).Biochem Pharmacol., 7:88-95.

P-380: IMIDAZOLE-LINKED MONO AND DI-KETOXIME DERIVATIVES ON GLIOBLASTOMA: SYNTHESIS AND IN VITRO STUDIES

[1,2] Kuzu, B., [3] Taspinar, F, [1,2] Menges, [4] Taspinar, MN., [5] Tasdemir, V., [6] Genc, H.,

[1] Van Yuzuncu Yil University, Department of Pharmaceutical Chemistry, Van, Turkey

[2] SAFF Chemical Reagents R&D Lab., Yyu-Teknokent, Van, Turkey

[3] Van Yuzuncu Yil University, Faculty of Medicine, Department of Physiology, Van, Turkey.

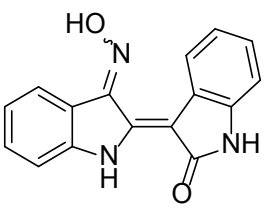
[4] Van Yuzuncu Yil University, Faculty of Medicine, Department of Medical Biology, Van, Turkey

[5] Scientific and Research Applied Center, Van Yuzuncu Yil University, Van, Turkey

[6] Van Yuzuncu Yil University, Faculty of Education, Chemistry Section, Van, Turkey

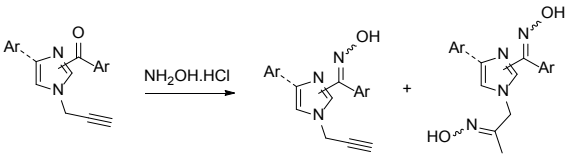
INTRODUCTION:

Indirubin-3'-oxime is a selective and potent inhibitor of CDKs. Indirubin and its derivatives showed antıproliferative effect at 10-20 μM concantration (1). With this effect, we want to sythesis a new imidazole-linked mono and di-ketoxime derivatives via unknown and simple method and to evaluate their antiproliferative effect on LN-405 cell lines.



indirubin-3'-oxime

MATERIALS AND METHODS:



Mono- and di-ketoxime derivatives were synthesized via condensation reaction. Both propargyl and carbonyl groups were affected by hydroxyl amine resulting in mono- or di-ketoxime derivatives.

RESULTS:

Various mono- and di-ketoxime derivatives were synthesized and selectivity for condensation with hydroxylamine was observed.

CONCLUSIONS:

We have found out an unknown and simple strategy for mono- and di-ketoxime derivatives. With this strategy, 18 different ketoxime compounds were synthesized which were subjected to MTT test with LN-405 cell line in order to observe their antiproliferative effects. We have assumed that we might reveal a good candidate for glioblastoma.

ACKNOWLEDGEMENTS:

This study was funded by Scientific and Technologic Research Agency of Turkey (TÜBİTAK) (grant numbers:115Z894)

REFERENCES:

1. Rahman A,(2013). In: Advances in Drug Targets, Volume 1, Bentham Books.

P-381: MLH1 -93G >A AND I219V POLYMORPHISMS AND SPORADIC COLORECTAL CANCER: A CASE-CONTROL STUDY IN TURKISH POPULATION

[1] Oztas, E., [1] Cilingir, U., [1] Akyuz, A., [2] Yanar, HT., [1] Ozhan, G.

[1]Istanbul University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, İstanbul, Turkey

[2]Istanbul University, Faculty of Medicine, Department of General Surgery, İstanbul, Turkey

INTRODUCTION:

Colorectal cancer (CRC) comprises approximately 10% of all cancers (1). DNA damage and altered DNA replication through the deregulation of related genes cause genomic instability in sporadic CRC. DNA repair is very complex; many factors play a role to ensure that the restoration of errors occurs during the transfer of genetic material. MutL homolog 1 (MLH1) is one of the vital DNA repair genes responsible for genomic stability (2, 3). Together with environmental factors, the genetic background may be associated with CRC development; thus, genetic polymorphisms are considered as risk factors. The

present prospective case–control study aimed to determine the association between 93G>A and I219V polymorphisms of MLH1 and CRC susceptibility in a Turkish population.

MATERIALS AND METHODS:

A prospective case-control study was conducted with Turkish participants. The genotyping of 158 patients and 164 controls was performed by PCR-RFLP. HWE was tested by using chi-square. Data comparisons were done by using Fisher's exact test; and, the odds ratios (ORs) and 95% confidence intervals (CIs) were estimated to evaluate the association between cases and controls. A two-tailed $p<0.05$ was considered to indicate a statistically significant difference.

RESULTS:

All samples were genotyped with high successful rate and concordance. Genotype distribution was found to be consistent with the HWE ($p>0.05$). The -93G>A and I219V minor allele frequencies were 0.494 and 0.469 in cases whereas 0.307 and 0.250 in controls, respectively. Individuals with A allele of -93G>A had about 2-fold (OR=1.92; 95% CI=1.22-3.04; $p<0.01$) and G allele of I219V had about 3-fold (OR=2.82; 95% CI=1.76-4.52; $p<0.01$) risk of developing sporadic CRC.

CONCLUSION:

The data is the first in understanding the influence of MLH1 on CRC risk in Turkish population, and suggested that -93G>A and I219V polymorphisms might be associated with sporadic CRC susceptibility. However, further studies conducted with different populations are needed.

ACKNOWLEDGEMENTS:

This work was unded by the Research Fund of Istanbul University (Project No. TLO-2016-23421).

References

1. Siegel et al., (2015). CA Cancer J Clin 65: 5-29.
2. Zhang et al., (2016). Oncol Lett 12: 4035-4040.
3. Savio et al., (2017). Clin Epigenetics 9: 26-39.

P-382: THE INHIBITORY EFFECTS OF PHENOTHIAZINE DYES ON B-SECRETASE

Biberoglu, K., Yuksel, M., Onder, S.,Tacal, O.

Hacettepe University, School of Pharmacy, Department of Biochemistry, Ankara, Turkey

INTRODUCTION:

Alzheimer's disease (AD) is a progressive, fatal neurodegenerative disorder characterized by accumulation of β-amyloid peptide (Aβ, 40-42 aa) in neuritic plaques, formation of neurofibrillary tangles caused by abnormal aggregation of tau protein and neural cell loss (1). Following the discovery of Aβ, which has a critical early role in AD pathogenesis, it soon became clear that the β-site amyloid precursor protein cleaving enzyme 1 (BACE1) is a prominent therapeutic target for the treatment of AD (1). Aβ, a peptide of 36-43 amino acids is derived from the amyloid precursor protein (APP) through sequential proteolytic cleavages by β- and γ-secretase enzyme activities (2). Recently, it was shown that methylene blue (MethB), which is a phenothiazine-structured compound acts as a modulator of BACE1 in a cell free system (3). The aim of our study was to investigate whether toluidine blue O (TBO) and azure B, a major metabolite of MethB, inhibit BACE1 activity directly.

MATERIALS AND METHODS:

The inhibitory effects of azure B and TBO on BACE1 activity were determined using a cell-free BACE1 assay kit which utilizes a fluorescence resonance energy transfer (FRET) technology. BACE1 inhibitor IV was used as a positive control for inhibition.

RESULTS:

Azure B and TBO significantly inhibited BACE1 activity in a dose-dependent manner. The inhibitory effects for 2.5 μM, 5 μM, 10 μM, 20 μM and 40 μM of azure B were 13%, 20%, 46%, %70 and 93%, respectively. On the other hand, the inhibitory effects for 2.5 μM, 5 μM, 10 μM, 20 μM and 40 μM of TBO, were 23%, 29%, 45%, %65 and 85% respectively.

CONCLUSIONS:

TBO and azure B were found to be potent inhibitors of BACE1. These results suggest that both compounds reduce β-secretase-mediated cleavage of APP and formation of Aβ.

ACKNOWLEDGEMENTS:

This study was supported by a grant from the Scientific Research Unit of Hacettepe University (HUBAB, TSA-2017-13929).

REFERENCES:

1. Querfurth HW, LaFerla FM (2010). New England Journal of Medicine, 362: 329-44.
2. Vassar et al., (2009). The Journal of Neuroscience, 29, 12787-12794.
3. Mori et al., (2014). The Journal of Biological Chemistry, 289:30303-30317.

P-383: INCREASED ANTICANCER EFFECTS IN HUMAN PROSTATE CANCER BY COMBINING VER-155008 AND CISPLATIN.

[1] Varol, K., [2] Ergul, M.

[1]Cumhuriyet University, Faculty of Pharmacy, Sivas, Turkey

[2]Cumhuriyet University, Department of Biochemistry, Sivas, Turkey

INTRODUCTION:

Prostate cancer is the most commonly diagnosed malignancy among men in the United States and the second leading cause of male cancer-related mortalities. Cisplatin is one of the most strong chemotherapeutic drugs for the treatment of many types of solid tumours. However, as prostate cancer cells exhibit resistance to cisplatin, it is not the first-line drug for prostate cancer chemotherapy (1, 2). Hsp70 is a chaperone that possess several physiological roles. This protein is also greatly overexpressed in tumor cells, contributing to resistance to chemotherapy and tumor cell survival (3). In the present study, we aimed to investigate the therapeutically chemosensitizing effect of Hsp70 inhibitor VER-155008 on cisplatin anti-tumour efficacy in prostate cancer cells PC-3.

MATERIALS AND METHODS:

The human androgen-independent prostate cancer cells were cultured and treated with serial concentrations (200- 100- 10- 1- 0,1 µM) of VER-155008 alone or in combination with cisplatin for 24 h. The anti-proliferative effect of cisplatin or cisplatin in combination with VER-155008 was assessed by XTT assay.

RESULTS:

Our results revealed that the VER-155008 significantly increased cisplatin cytotoxicity in the androgen-independent prostate carcinoma cell lines PC-3. The IC50 value of cisplatin was calculated as 68,5 µM in the absence of VER-155008. When cisplatin was combined with VER-155008 the IC50 value of combination was reduced to 9,37 µM at 24 h.

CONCLUSIONS:

In conclusion, our findings showed that VER-155008 increases the sensitivity of PC-3 cells to cisplatin-induced growth inhibition. This result suggests that VER-155008 in combination with cisplatin may serve as a potentially useful therapeutic strategy for prostate cancer patients.

ACKNOWLEDGEMENTS:

This study was supported by the Cumhuriyet Universtiy BAP (Project No: Ecz-045).

REFERENCES:

1. Li QQ, Wang G, Reed E, Huang L, Cuff CF (2010). Basic Clin Pharmacol Toxicol., 107:868-76.
2. Liotti A, Cosimato V, Mirra P (2018). J Cell Physiol. 2018:1-11.
3. Reikvam H, Nepstad I, Sulen A et all. (2013). Expert Opin Investig Drugs., 22:551-63.

P-384: ATTENUATION OF TESTIS DAMAGE IN STREPTOZOTOCIN-INDUCED DIABETIC RATS BY VACCINIUM MYRTILLUS L. EXTRACT

[1] Berkoz, M., [2] Kahraman, T., [3] Yildirim, M., [4] Allahverdiyev, O., [3] Yalin, S., [1] Saeed, KM., [5] Turel, I.

[1] Yuzuncu Yıl University, Faculty of Pharmacy, Department of Biochemistry, Van, Turkey

[2] Karabuk University, Faculty of Medicine, Department of Medical Biochemistry, Adıyaman, Turkey

[3] Mersin University, Faculty of Pharmacy, Department of Biochemistry, Mersin, Turkey

[4] Yuzuncu Yıl University, Faculty of Pharmacy, Department of Pharmacology, Van, Turkey

[5] Abant İzzet Baysal University, Faculty of Medicine, Department of Medical Pharmacology, Bolu, Turkey

INTRODUCTION:

Vaccinium myrtillus L. is a traditional Eurasian medicine that has been used in the treatment of diabetes (1-3). However, the mechanism of Vaccinium myrtillus L. activity is still unclear. This study aims to examine the effect of Vaccinium myrtillus L. on the oxidative stress in testis tissues of experimental diabetic rats.

MATERIALS AND METHODS:

In this study, 28 rats were disturbed into 4 different groups. Group I was control group, group II was diabetes group which was administered single dose of streptozotocin (45 mg/ kg), in Group III, rats were not made diabetic but given extract of Vaccinium myrtillus L. (1.2 g/kg) by gavage for 21 days; Group IV rats were made diabetic and given extract of Vaccinium myrtillus L. (1.2 g/kg) by gavage for 21 days. After these practices, all the animals were sacrificed, and the testis tissues of each animal were isolated. These tissues were homogenized and superoxide dismutase (SOD), catalase (CAT) activities and malondialdehyde (MDA) and glutathione (GSH) levels were examined.

RESULTS:

In our study, MDA levels increased, CAT, SOD activities and GSH level decreased in group II comparing with group I ($p<0.05$). Furthermore, MDA levels decreased, CAT, SOD activities and GSH level increased in group IV comparing with group II ($p<0.05$).

CONCLUSIONS:

According to these results, it can be suggested that Vaccinium myrtillus L. was found to reduce the oxidative stress. As a result, we can suggest that extract of Vaccinium myrtillus L. may be used for the treatment of diabetes.

REFERENCES:

1. Sanchez-Villavicencio ML, Vinqvist-Tymchuk M, Kalt W, Matar C, Alarcon Aguilar FJ, Escobar Villanueva MD, Haddad PS (2017). BMC Complementary and Alternative Medicine, 17:24-32.
2. Bunea A, Rugină D, Sconţa Z, Pop RM, Pintea A, Socaciu C, Tăbăran F, Grootaert C, Struijs K, VanCamp J (2013). Phytochemistry,95:436-444.
3. Song Y, Huang L, Yu J (2016). Journal of Neuroimmunology, 301:1-6.

P-385: SYNTHESIS AND EVALUATION OF NEW 2-SUBSTITUTED BENZOXAZOLE DERIVATES AS ANTICANCER AGENTS

[1] Aksoy, MO., [2] Kaya Cavusoglu, B., [1] Akalın Ciftci, G.,[2] Yurttas, L.

[1] Anadolu University, Faculty of Pharmacy, Department of Biochemistry, Eskisehir, Turkey

[2] Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskisehir, Turkey

INTRODUCTION:

Benzoxazoles have been known to act as potential anticancer compounds. Recently, different authors have reported cytotoxic, anticancer or apoptotic potential of these compounds. (1,2). In this study, some new 2-subtituted benzoxazole derivatives were synthesised and evaluated for their cytotoxic effects on A549 human lung adenocarcinoma cell line.

MATERIALS AND METHODS:

The structural elucidation of the compounds was performed by 1H-NMR, 13C-NMR and LC-MS/MS spectral data and elemental analyses. A549 cell lines were used in the studies. The cytotoxic activities of the tested compounds were determined by cell proliferation analysis using standard MTT assay. Detection of apoptosis was performed using Annexin V-FITC apoptosis detection kit BD, Pharmingen according to the manufacturer's instruction.

RESULTS:

According to assay results, The most effective cytotoxic agent against A549 cancer cell line was found as compounds 4, 5, 7, 8, 9, 10 (IC50 values were < 3.9, 10,33±1.53, 11,67±0.58, 5.00±1.00, <3.9, 4,5±0.71 µg/mL respectively) followed by compounds 6 and 11 (IC50 values were 22,67±2.52, and 23.00±2.00 µg/mL respectively). However, compounds 1, 2 and 3 were the less active compounds on A549 cell line (IC50 values were as >500, 170.0±34,64, 58,33±2.89 µg/mL respectively) compared to cisplatin (19,00±1,41 respectively). After 24h incubation period, the apoptotic effects of compounds 4,5,7, 8, 9 and 10 were increased on A549 cells based on Annexin V-PI binding capacities in flow cytometry.

CONCLUSIONS:

According to these findings, compounds 4 (3-pyridyl substituted), 5 (3-indolyl substituted) , 7 (4-methylphenyl substituted) , 8 (4-methoxyphenyl substituted), 9 (4-chlorophenyl substituted), 10 (4-fluorophenyl substituted) were the most effective anticancer compounds among these novel 2-substituted benzoxazole derivatives.

REFERENCES:

1. Silverstein A, Silverstein V, Silverstein Nunn, L (2006). Cancer, Conquering a Deadly Disease; A Division of Lerner Publishing Group: Minneapolis, MN, USA pp. 9–11.
2. Almeida CA, Barry SA (2010). Cancer: Basic Science and Clinical Aspects; Wiley-Blackwell: Hoboken, NJ, USA pp. 2–3.

P-386: PROTECTIVE ROLE OF FERULIC ACID AGAINST LIPID PEROXIDATION AND PROTEIN OXIDATION INDUCED BY IMIDACLOPRID IN LIVER TISSUE OF CYPRINUS CARPIO

[1] Ozkan Yilmaz, F., [1] Onder, S., [1] Ozluer Hunt, A., [2] Yildirim, M., [3] Berkoz, M., [2] Yalin, S.

[1] Mersin University, Faculty of Fisheries, Mersin, Turkey

[2] Mersin University, Faculty of Pharmacy, Mersin, Turkey

[3]Van Yüzüncüyıl University, Faculty of Pharmacy, Van, Turkey

INTRODUCTION:

The fact that oxidative stress plays an important role in many diseases has increased interest in studies on antioxidants. Among natural antioxidants, polyphenols play a very important role (1). Phenolic acids are the simplest phenolic compounds in plants. It consists of two subgroups, namely hydroxybenzoic acid and hydroxycinnamic acid, and is the precursor of flavonoids. Numerous studies have been carried out to reveal the antioxidant activity of phenolic compounds in plants (2). Pesticides that are widely used in agriculture and pose a great threat to fish by entering aquatic environment, catalyzing oxidative reactions; lead to formation of reactive oxygen species such as hydrogen peroxide, superoxide and hydroxyl radical. These radicals are highly reactive compounds which cause the oxidation and degradation of

important biological molecules such as proteins and lipids. Imidacloprid (IMI) is a neurotoxic insecticide, competitively similar to nicotine and competes with acetylcholine for its receptor site. Malondialdehyde (MDA) is a major and most studied peroxidation product. The most commonly measured product of protein oxidation is protein carbonyls. In this study, the protective effect of ferulic acid (FA) against oxidative stress was investigated in a 2.80 mg/L sublethal concentration of IMI, a neonicotinoid insecticide, in Cyprinus carpio. For this purpose, MDA and protein carbonyl levels of liver tissue were determined in fish fed with FA supplemented feed.

MATERIALS AND METHODS:

The fish treated with 2.80 mg/L imidocloprid were fed with 5% FA supplemented feed. Liver tissue samples were taken on days 4 and 10 of the study, which included control, FA, IMI and IMI + FA groups. Tissue MDA level was determined according to Yagi method. The identification of carbonyl groups formed on oxidative stress-affecting proteins has been reported by Levine et al. method.

RESULTS:

Liver tissue MDA and PCO levels were increased compared to control with IMI effect during the experimental periods. No statistical difference was found when the individuals of the FA + IMI group had enzyme activity on the 4th day compared to the IMI group. On the 10th day, however, it was determined that the enzyme activity of the FA application and the MDA and PCO amounts were improved on the 10th day.

CONCLUSIONS:

Ferulic acid (4-hydroxy-3-methoxycinnamic acid) is a phenolic compound found in plant tissues during phenylalanine and tyrosine metabolism. In some countries, it has been approved as a food additive to prevent oxidation because it has an active role on free radicals. FA has proven to be a powerful membrane antioxidant and end free radical chain reactions.

ACKNOWLEDGEMENTS:

This study was supported by Mersin University, Department of Scientific Research Projects (BAP-2017-2-TP2-2522)

REFERENCES:

1. Crozier A, Jaganath IB, Clifford MN (2009). Natural Product Reports, 26, (8), 1001-1043.
2. Masek A, Chrzescijanska E, Latos M, Zaborski M (2016). International Journal of Electrochemical Science, 11, 8848-8860.

P-387: THE EFFECTS OF RADIOFREQUENCY ELECTROMAGNETIC RADIATION FROM CELL PHONE CAUSES OXIDATIVE STRESS ON HEART TISSUE IN WISTAR ALBINO RATS

[1] Yildirim, M., [2] Arslan, B., [3] Berkoz, M., [2] Aras, N., [1] Yalin, S.

[1]Mersin University, Department of Biochemistry, Mersin, Turkey

[2]Mersin University, Department of Medical Biology and Genetics, Mersin, Turkey

[3]Van Yüzüncü Yıl University, Department of Biochemistry, Faculty of Pharmacy, Van,Turkey

INTRODUCTION:

Cell phones have become an integral part of everyday life. As cell phone usage has become more widespread, concerns have increased regarding the harmful effects of radiofrequency electromagnetic radiation from these devices. The current study was undertaken to investigate the effects of the emitted radiation by cell phones on heart tissue (1)

MATERIALS AND METHODS:

Thirty-seven female Wistar albino rats were divided into three groups; study group (n=9), sham group (n=9) and control group (n=9). The rats in the study group were exposed to 1800 MHz RF-EMF (Radiofrequency electromagnetic field). Malondialdehyde (MDA, an index of lipid peroxidation) were used as markers of oxidative stress-induced heart impairment. Superoxide dismutase (SOD), catalase (CAT), paraoxonase (PON), arylesterase (ARE) and glutathione peroxidase (GSH-Px) activities were studied to evaluate the changes of antioxidant status.

RESULTS:

In the 1800 MHz RF-EMF exposed group, while tissue MDA level increased, SOD, CAT and PON, ARE activities were reduced.

CONCLUSIONS:

These results show that cell phone radiation can be reason free radical mediated oxidative heart impairment in rats.

REFERENCES:

1. Oyewopo et al., (2017). Andrologia 49:10.

P-388: MOLECULAR, BIOCHEMICAL AND IN SILICO ANALYSES OF COMMERCIAL AND NOVEL PHENOTHIAZINES AS ANTICANCER AGENTS

[1,2] Yaman, M., [1] Tiryaki, RS., [4] Zengin, F., [4] Kisla, MM., [1] Bayazeid, O., [1,2] Keskus, AG., [4] Ates Alagoz, Z., [1,2,3] Konu O.

[1] Bilkent University, Department of Molecular Biology and Genetics, Ankara, Turkey

[2] Bilkent University, Neuroscience Program, Ankara, Turkey

[3] Bilkent University, UNAM, Ankara, Turkey

4Ankara University, Department of Pharmaceutical Chemistry, Ankara, Turkey

INTRODUCTION:

Hepatocellular carcinoma (HCC), is one of the deadliest cancer types, where the treatment options are limited. Therefore, it is important to design and test compounds in HCC cells with effects against cancer growth and metastasis. We have synthesized and identified several promising phenothiazines with anticancer properties in HCC. In this study we present molecular effects and biochemical activities of selected phenothiazines with respect to different signaling pathways including cholesterol biosynthesis, cell division, RNA processing along with cholinesterase activity. In silico structural comparisons also have been made.

MATERIALS AND METHODS:

Commercial phenothiazines (phenothiazine, perphenazine, prochlorperazine dimaleat, trifluoperazine HCl) were purchased from SIGMA while novel derivatives were synthesized at Ankara University, Turkey. qRT-PCRs were performed for selected genes with gene specific primers after exposure to 10 μM and 20 μM of the prioritized compounds for 24 hours in SKHep1 and Hep3B cell lines. Different target prediction softwares such as Swiss Target Prediction (1) and SPiDER (2) were used to identify molecular targets of the phenothiazines. Obtained similarity scores were used for hierarchical clustering with Ward linkage in MATLAB ®. Cholinesterase activity was studied colorimetrically using AchE assay.

RESULTS:

In silico results indicated acetylcholinesterase as one of the top consensus molecular targets. Comparison of the most active molecules indicated that the piperazine ring might be important for acetylcholinesterase activity. This was parallel with our results showing that cholinesterase inhibitory activity of some of the novel derivatives were relatively higher than many of the commercial phenothiazines. Moreover, gene expression analyses have shown significant effects on expression of several genes, e.g., SQLE, DDIT3, SRSF7, NIP7, LSS, CCNE2 and RRM2 with dose- and cell-line dependent differences. Currently, we are focusing on molecular and biochemical analyses of other newly synthesized molecules before finalizing lead compounds for high throughput transcriptomics.

CONCLUSIONS:

Studied phenothiazines exhibited important modulations in cellular signaling and activity in HCC cell lines and in silico studies have opened new avenues for our future studies.

ACKNOWLEDGEMENTS:

This study was supported by TUBITAK (Grant No.: SBAG-116Z388) and Fikriye Zengin has been supported by a TUBITAK-BIDEB fellowship.

REFERENCES

1. Gfeller et al., (2013). Bioinformatics 29(23):3073-9.
2. Reker et al., (2014). Proceedings of the National Academy of Sciences 111(11):4067-4072.

P-389: CYTOTOXIC EFFECTS OF PLK1 INHIBITORS RO3280 AND SBE 13 HYDROCHLORIDE ON BREAST CANCER CELLS MDA-MB-231.

[1] Ergul, M., [2] Ergul, M., [3] Altun, A.

[1]Cumhuriyet University, Department of Biochemistry, Sivas, Turkey

[2]Cumhuriyet University, Department of Pharmacology, Sivas, Turkey

[3]Cumhuriyet University, Department of Medical Pharmacology, Sivas, Turkey

INTRODUCTION:

Cancer is one of the most important health issues worldwide. Conventional treatments, such as chemotherapy, surgery, and radiotherapy possess several side effects (1, 2). To overcome this hurdle, targeted treatment has been widely employed to enhance therapeutic efficacies and reduce systemic toxicity of pharmaceutical agents. Polo-like kinases (PLKs) are a family of serine/threonine protein kinases and consist of five isoforms. Among them, PLK1 plays an important role in the initiation, maintenance, and completion of mitosis. This protein also overexpressed in many cancers and this high-level expression causing poor prognosis in cancer patients (3). Therefore, specific inhibition of PLK1 in tumor cells is an important strategy in the treatment of cancer. In the present study, we aimed to investigate the antiproliferative effects of Ro380 and SBE 13 hydrochloride on MDA-MB-231 cells.

MATERIALS AND METHODS:

MDA-MB-231 cells were cultured and treated with different concentrations (100- 50- 25- 12.5- 6.25-

3.12- 1.56 μM) of Ro380 and SBE 13 hydrochloride. The antiproliferative activity of the inhibitors was evaluated using the XTT assay.

RESULTS:

Our findings showed that Ro380 and SBE 13 hydrochloride exposure inhibited MDA-MB-231 cell proliferation ($p<0.05$) in a dose-dependent manner compared to the control cells. The IC50 of Ro380 and SBE 13 hydrochloride in MDA-MB-231 cell line were calculated as 11.29 μM and 21.51 μM after 24 h of treatment, respectively.

CONCLUSIONS:

In conclusion, our cytotoxicity results clearly revealed that the Ro380 is more toxic than the SBE 13 hydrochloride on MDA-MB-231 cells. However, further studies are needed to be able to utilize Ro380 and SBE 13 hydrochloride derivatives in breast cancer.

ACKNOWLEDGEMENTS:

This study was supported by the Cumhuriyet Universtiy BAP (Project No: Ecz-045).

REFERENCES:

1. Tayoub G, Al-Odat M, Amer A, Aljapawe A, Ekhtiar (2018). Iran J Med Sci, 43:52-64.
2. Birjandiana E, Motameda N, Yassa N (2018). Iran J Pharm Res, 17:307-316.
3. Liu Z, Sun Q, Wang X (2017). PLK1, A Potential Target for Cancer Therapy, 10:22-32.

P-390: CYTOTOXIC EFFECTS OF PLK1 INHIBITORS RO3280 AND SBE 13 HYDROCHLORIDE ON DU 145 AND SH-SY5Y CELL LINES.

[1] Ergul, M., [2] Ergul, M., [3] Altun, A.

[1]Cumhuriyet University, Department of Biochemistry, Sivas, Turkey

[2]Cumhuriyet University, Department of Pharmacology, Sivas, Turkey

[3]Cumhuriyet University, Department of Medical Pharmacology, Sivas, Turkey

INTRODUCTION:

Cancer is a serious life-threatening disease and the second-leading cause of death worldwide after cardiovascular diseases (1). PLK1 plays multiple roles in the cell cycle and highly expressed in most of human cancers, furthermore, its overexpression is associated with poor prognosis in cancer patients. Thus, it has been suggested that PLK1 could be an attractive target for cancer therapy (2). This study aimed to investigate the antiproliferative effects of Ro380 and SBE 13 hydrochloride on DU 145 prostate and SH-SY5Y neuroblastoma cells.

MATERIALS AND METHODS:

DU145 and SH-SY5Y cells were cultured and treated with different concentrations (100- 50- 25- 12.5- 6.25- 3.12- 1.56 μM) of Ro380 and SBE 13 hydrochloride. The antiproliferative activity of the inhibitors was evaluated using the XTT assay.

RESULTS:

Our results demonstrated that the Ro380 and SBE 13 hydrochloride exposure inhibited DU 145 and SH-SY5Y cell proliferation ($p<0.05$) in a dose-dependent manner compared to the control cells. The IC50 of Ro380 in DU 145 and SH-SY5Y cell lines were calculated as 1.84 μM and 10.97 μM, respectively. The IC50 of SBE 13 hydrochloride in DU 145 and SH-SY5Y cell lines were calculated as 1.97 μM and 13.51 μM after 24 h of treatment, respectively.

CONCLUSIONS:

In conclusion, our cytotoxicity results clearly revealed that the Ro380 is more toxic than SBE 13 hydrochloride on DU 145 and SH-SY5Y cells. However, further studies are needed to be able to utilize Ro380 and SBE 13 hydrochloride derivatives in prostate and neuroblastoma cancer.

ACKNOWLEDGEMENTS:

This study was supported by the Cumhuriyet Universtiy BAP (Project No: Ecz-045).

REFERENCES:

1. Jian, B, Zhang H, Han C, Liu J (2018). Steud, 23:1-11.
2. Liu Z, Sun Q, Wang X (2017). PLK1, 10:22-32.

P-391: THE EFFECT OF FUNCTIONALIZED PYRROLIDINE - INDOLE HYBRID HETEROCYCLES ON VEGF IN MCF-7 CELLS

[1] Canacankatan, N., [2] Belveren, S., [2] Poyraz, S., [3] Kibar, D., [3] Yetkin, D., [3] Yilmaz, SN. [2] Dondas, HA.

[1]Mersin University, Faculty of Pharmacy, Department of Biochemistry, Mersin, Turkey.

[2]Mersin University, Faculty of Pharmacy, Department of Analytical Chemistry, Mersin, Turkey.

[3]Mersin University, Faculty of Medicine, Department of Histology and Embryology, Mersin, Turkey.

INTRODUCTION:

Breast cancer is the most common metastatic and invasive cancer in women worldwide, so that prolongation of survival and improvement of quality of the life is the biggest goal in breast cancer (1). MCF-7 cell lines are used for breast cancer studies because of their several ideal properties specific to mammary epithelium and retaining their estrogen sensitivity (2). The aim of this study was to investigate functionalized pyrrolidine-indole hybrid heterocycles (3,4) on vascular endothelial growth factor (VEGF),

one of the most important mediators of angiogenesis in *MCF-7 cell lines.*

MATERIALS AND METHODS:

Functionalized pyrrolidine-indole hybrid compounds, 1a and 1b were synthesized as part of our previous studies and characterized by analytical techniques. The compounds were screened for their *cytotoxicity on MCF-7 cell lines.* VEGF levels were assayed respect to the manufacturer's guidance. The results were stated in ng/mg protein.

RESULTS:

A statistically significant increase in VEGF level was observed in the DMSO (solvent) 24h group compared to the Control. VEGF levels significantly decreased in both 1a and 1b 24h groups compared with the DMSO 24h groups ($p<0.05$). Although VEGF levels also decreased in both 1a and 1b 48h groups compared with the DMSO 48h groups, these results were not significant.

CONCLUSIONS:

The obtained results displayed that functionalized pyrrolidine - indole hybrid compounds 1a and 1b may be considered as *anti-angiogenic agents*. Further studies needed to be carried out different solvents.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Mersin University, Research Foundation (BAP 2015-AP2-1342)

REFERENCES:

1. Senkus E, Lacko A. (2017). The breast, 31:309-317.
2. Lee AV, Oesterreich S. et al. (2015). J Natl Cancer Inst, 107:1-4.
3. Malose et al., (2016). Bioorganic & Medicinal Chemistry, 24:4576–4586.
4. Arun et al., (2014). European Journal of Medicinal Chemistry, 74: 50-64.

P-392: INVESTIGATION OF POLYPHENOL CONTENTS AND ANTIOXIDANT ACTIVITIES OF LACTARIUS DELICIOUS AND LACTARIUS SALMONICOLOR MUSHROOMS

[1] Shomali, N., [1] Onar, O., [1] Akata, I.,[1] Yildirim, O.

Ankara University, Faculty of Science, Department of Biology, Ankara, Turkey

INTRODUCTION:

Edible mushrooms have been part of the human diet for several centuries. It is the total diet or overall eating pattern that is most important in disease prevention and achieving good health. It is better to eat a diet with variety than to concentrate on individual foods as the key to good health.Nowadays there is a growing interest in new drugs against secondary metabolites derived from fungi and for the discovery of precursor compounds. These bioactive components are becoming popular sources of natural antioxidant, antitumor, antiviral, antimicrobial and immunomodulatory agents.

MATERIALS AND METHODS:

In this study, the ethanol extracts of Lactarius delicious and Lactarius salmonicolor species were analyzed for the polyphenolic contents by using spectrophotometrically methods. The free radical scavenging activities of extracts were evaluated by DPPH assay. Besides, the mushroom extract effects were examined on the glutathione peroxidase (GPx) enzyme activity by kinetic assay (1).

RESULTS:

Ethanol extract of L. salmonicolor has been shown the highest total of phenolic compounds with 8.615±0.0008 mg GAE/g and L. delicious also has been shown the highest amount of flavonoid contents with 7.822 ±0.0041 mg QE/g values. The highest DPPH radical scavenging activity was measured as 80% at 10 mg/mL concentration for ethanol extract of L. delicious. Also, the best activity profile for GPx was observed with the crude ethanol extract of L. delicious at 2.5 mg/mL concentration.

CONCLUSIONS:

L. delicious may be considered as a good source of functional food for the detoxification and antioxidant defense systems.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (116Z125)

REFERENCES:

1. Paglia DE, Valentine WN (1967). J Lab Clin Med, 70:158-69.

P-394: INVESTIGATION OF THE EFFECT OF VACCINIUM MYRTILLUS L. ON OXIDATIVE STRESS IN LUNG TISSUE OF DIABETIC RATS

[1] Yalin, S., [2] Berkoz, M., [3] Kahraman, T., [1] Yildirim, M., [4] Allahverdiyev, O., [2] Saeed, KM., [5] Turel, I.

[1] Mersin University, Faculty of Pharmacy, Department of Biochemistry, Mersin, Turkey

[2] Yuzuncu Yıl University, Faculty of Pharmacy, Department of Biochemistry, Van, Turkey

[2] Karabuk University, Faculty of Medicine, Department of Medical Biochemistry, Adıyaman, Turkey

[4] Van Yuzuncu Yıl University, Faculty of Pharmacy, Department of Pharmacology, Van, Turkey

[5] Abant İzzet Baysal University, Faculty of Medicine, Department of Medical Pharmacology, Bolu, Turkey

INTRODUCTION:

Bilberry fruit extracts have been studied for the prevention and treatment of chronic pathologies, such as diabetes, cardiovascular disease and obesity. This study aims to examine the effect of Vaccinium myrtillus L. on the oxidative stress in lung tissues of experimental diabetic rats.

MATERIALS AND METHODS:

In this study, 28 rats were disturbed into 4 different groups. Group I was control group, group II was diabetes group which was administered single dose of streptozotocin (45 mg/ kg), in Group III, rats were not made diabetic but given extract of Vaccinium myrtillus L. (1.2 g/kg) by gavage for 21 days; Group IV rats were made diabetic and given extract of Vaccinium myrtillus L. (1.2 g/kg) by gavage for 21 days. After these practices, all the animals were sacrificed, and the lung tissues of each animal were isolated. Lung tissues were homogenized and superoxide dismutase (SOD), catalase (CAT) activities and malondialdehyde (MDA) and glutathione (GSH) levels were examined.

RESULTS:

In our study, MDA levels increased, CAT, SOD activities and GSH level decreased in group II comparing with group I ($p<0.05$). Furthermore, MDA levels decreased, CAT, SOD activities and GSH level increased in group IV comparing with group II ($p<0.05$).

CONCLUSIONS:

According to these results, it can be suggested that Vaccinium myrtillus L. was found to reduce the oxidative stress. As a result, we can suggest that extract of Vaccinium myrtillus L. may be used for the treatment of diabetes.

REFERENCES:

1. Sanchez-Villavicencio ML, Vinqvist-Tymchuk M, Kalt W, Matar C, Alarcon Aguilar FJ, Escobar Villanueva MD, Haddad PS (2017). BMC Complementary and Alternative Medicine, 17:24-32.
2. Bunea A, Rugină D, Sconţa Z, Pop RM, Pintea A, Socaciu C, Tăbăran F, Grootaert C, Struijs K, VanCamp J (2013). Phytochemistry, 95:436-444.
3. Song Y, Huang L, Yu J (2016). Journal of Neuroimmunology, 301:1-6.

P-395: EFFECT OF COMBINED RADIOTHERAPY AND IMIPRAMINE ON OXIDATIVE STRESS IN PROSTATE CANCER CELLS

[1] Barlaz Us, S. [2] Yildirim, M., [3] Yetkin, D., [2] Yalin, S., [4] Sogut, F., [5] Yilmaz, SN., [6] Comelekoglu, U

[1] Mersin University, Faculty of Medicine, Department of Radiation Oncology, Mersin, Turkey

[2]Mersin University, Faculty of Pharmacy, Department of Biochemistry, Mersin, Turkey

[3]Mersin University, Institute of Advanced Technology Research and Application, Mersin, Turkey

4Mersin University, Vocational School Of Health Services, Mersin, Turkey

5Mersin University, Faculty of Medicine, Department of Histology-Embryology, Mersin, Turkey

6Mersin University, Faculty of Medicine, Department of Biophysics, Mersin, Turkey

INTRODUCTION:

Radiotherapy (RT) has been widely used as a curative treatment for local prostate cancer (1). However, prostate cancer radioresistance causes in a number of patients, leading to cancer recrudesce. The combination of pharmacologic drugs and RT in prostate cancer increases the effectiveness of RT with minimal side effects (2). Imipramine, a tricyclic antidepressant, when present in the growth medium of Eag1-expressing tumor cells, and slows cell proliferation by blocking Eag 1 K+ channel (3). In this study, it was aimed to investigate the radiosensitive effect on RT of imipramine.

MATERIALS AND METHODS:

In this study, DU-145 prostate cancer cell lines were used. The cells were divided into 4 groups (n=4 each group). Group 1 is the control group. Group 2 is the imipiramine group (1 μM imipramine was given to the prostate cells). Group 3 is the RT group (6 Gy radiation as a single fraction) (4). Group 4 is the RT+ imipramine group (6 Gy radiotherapy and 1 μM imipramine). Cells were incubated 24 hours after RT with imipramine. Superoxide dismutase (SOD) and catalase (CAT) activities and malondialdehyde (MDA) levels were measured 72 hours after incubation in all groups.

RESULTS:

In all experimental groups, SOD and CAT activity significantly decreased compared to control group ($p<0.05$). MDA level was significantly higher in all experimental groups than control group ($p<0.05$). In the RT+imipramine group, MDA level significantly lower than imipramine and RT groups and significantly higher than control group ($p<0.05$).

CONCLUSIONS:

Our findings have suggested that individual treatment of radiotherapy and imipramine enhanced oxidative stress than combined treatment of RT and imipramine. Another important finding of this study was that imipramine increased oxidative stress in DU 145 cell lines as much as radiotherapy. This result suggests that imipramine may be an alternative to radiotherapy in the treatment of prostate cancer.

ACKNOWLEDGEMENTS:

This study was supported by Mersin University (Project No: 2017-2-AP4-2537)

REFERENCES:

1. Siegel R, Naishadham D, Jemal, A (2013). Cancer Statistics. Cancer J Clın., 63:11–30.
2. Iwamoto, Ishii K, Kanda H, et.al (2017). Combination treatment with naftopidil increases the efficacy of radiotherapy in PC-3 human prostate cancer cells. J Cancer Res Clin Oncol. Doi: 10.1007/s00432-017-2367-9.

P-396: INVESTIGATION OF GGT1 AND GGT6 MRNA EXPRESSIONS IN PATIENTS WITH BREAST CANCER

[1] Yardim Akaydin, S., [1] Miser Salihoglu, E., [1] Ramadan, SS., [2] Karanlik, H., [3] Demokan, S.

1 Gazi University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey
2 Istanbul University, Institute of Oncology, Department of Surgery, Istanbul, Turkey
[3] Istanbul University, Oncology Institute, Department of Basic Oncology, Istanbul, Turkey

INTRODUCTION:

Besides GGT1, pre-genome researches had showed that the human genome contains additional related genes or sequences. One of these genes, GGT6 (formerly rat ggt6 homologue) had limited amino acid sequence homology to GGT1 and its function as an enzyme has not yet been described. The aim of this study was to evaluate the gene expressions of GGT1 and GGT6 in breast cancer. Also, we aimed to investigate the relationship of GGT genes with GGT enzyme activity.

MATERIALS AND METHODS:

Normal and tumor tissue samples were collected from 58 patients diagnosed with breast cancer. As controls, 8 healthy persons admitted to the clinic for breast reduction surgery were also included to the study. mRNA expressions of GGT1 and GGT6 in normal and tumor tissue samples of breast cancer patients and healthy controls examined by qRT-PCR method. In addition, GGT enzyme activity in serum samples was measured by spectrophotometric method.

RESULTS:

In contrast to GGT1, GGT6 mRNA expressions were higher in tumor tissues than those in normal tissues ($p=0.020$ for GGT1 and $p=0.045$ for GGT6). Also, GGT enzyme activity was significantly higher in patients than those in controls ($p<0.05$). We did not find any correlation between GGT and GGT genes.

CONCLUSIONS:

Although the function is unknown, we believe that GGT6, which shows significant mRNA expressions in tissue samples of most patients, needs to be further investigated. It is not surprising that there is no correlation between GGT activity and tissue GGT expressions because serum GGT enzyme levels are predominantly liver-derived.

ACKNOWLEDGEMENTS:

This study was supported by a grant of GUBAP (02/2017-02)

REFERENCES:

1. Heisterkamp N, Groffen J, et al. (2008). Human Genetics, 123:321-332.
2. Meister et al., (1981). Methods in Enzymology, 77:237-253.
3. Yardim Akaydin et al., (2017). Fabad Journal of Pharmaceutical Sciences 42(1):21-28.

P-397: THE ROLES OF HSSB1 AND HSSB2 IN THE DNA DAMAGE CHECKPOINT SIGNALLING

[1] Bereketoglu, S., [2] Sancar, A.

[1] Ankara University, Faculty of Science, Department of Biology, Ankara, Turkey

[2] The University of North Carolina at Chapel Hill, Department of Biochemistry and Biophysics, North Carolina, USA

INTRODUCTION:

Single strand DNA binding proteins (SSBs) have crucial roles in the DNA metabolism (1). A well-known SSB called Replication Protein A (RPA) is the major player in initiating the DNA-damage checkpoint signaling cascade (2, 3). Two novel SSB proteins, hSSB1 and hSSB2, were discovered by sequence homology to an archeal SSB (4). It was found that cells deficient of hSSB1 cannot phosphorylate Chk1, a step required to transduce checkpoint signals in response to IR induced DNA damage (4). In order to determine the role hSSB1 and hSSB2 play in UV-induced DNA damage checkpoint pathway, an in vitro checkpoint system was developed in which Chk1 is phosphorylated in an ATR-dependent manner in the presence of TopBP1 and ATP. In this system, ATR kinase activity is stimulated by TopBP1 and this effect is improved by single strand DNA (ssDNA) addition to the reaction.

MATERIALS AND METHODS:

To address the question, firstly His tagged hSSB1 and hSSB2 were purified using an Ni-NTA affinity column and their ability to bind ssDNA was tested by EMSA using 5' end labeled oligomers, d30T and d30AC. Then, Chk1 phosphorylation in the presence of hSSB1 and hSSB2 was assayed using a combination of kinase assay and immunoblotting with Chk1 phospho-S345 antibody.

RESULTS:

Our results showed that hSSB1 efficiently binds to ssDNA. It was demonstrated that hSSB1 does not improve Chk1 phosphorylation in response to UV-induced damage. hSSB2 on the other hand was found to inhibit phosphorylation in response to UV damage.

CONCLUSIONS:

These results indicate that, unlike IR-induced damage, hSSB1 is not directly involved in UV-induced damage response. Moreover, hSSB2 might interfere and alleviate ATR-kinase activity on Chk1 phosphorylation to initiate UV-damage response. Further experiments are requied to evaluate the specific roles of both hSSB1 and hSSB2.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Ministery of National Education

REFERENCES:

1. Coverly D, Kenny MK, Munn M, Rupp WD, Lane DP, Wood RD (1991). Nature, 349:538-541.
2. Wu X, Yang Z, Liu Y, Zou Y (2005). Biochemistry J 391(Pt 3):473:480.
3. Zou L, Elledge SJ (2003). Science, 300:1542-48.
4. Richard DJ, Bolderson E, White MF, Khanna KK (2008). Nature, 453:677-681.

P-398: PREDICTIVE VALUE OF SERUM INHIBIN B CONCENTRATION IN WOMEN WITH UNEXPLAINED INFERTILITY

[1] Turan, T., [2] Pekel, A., [2] Iltemir Duvan, ZC., [1] Gonenc, A.

[1] Gazi University, Department of Biochemistry, Ankara, Turkey

[2] Medical Park Hospital, Obstetrics And Gynaecology, Ankara, Turkey

INTRODUCTION:

Infertility is defined as the inability to obtain a pregnancy for at least one year, despite desiring of couples to have children and having regular unprotected sexual intercourse (1). Unexplained infertility is a group under infertility and had a share of 15-30%. Our knowledge is quite less in the unexplained infertility cases because of no reason to explain infertility. Inhibin B, is accepted as a marker to show the follicular growth and ovarian reserve. It is known that, serum inhibin B concentration is negatively correlate with FSH level, which have been shown to have an association with decreased oocyte quality and fertility (2). Serum Inhibin B concentration can be a useful tool in the management of unexplained infertility. Thus, it was aimed to characterize hormone levels in women with unexplained infertility, and measure the serum inhibin B concentration in both patients and controls in order to determine their roles in unexplained infertility.

MATERIALS AND METHODS:

In this study, 47 unexplained infertility patients and 41 controls, matched for age (32.2±4.7, 30.4±4.8, respectively), were enrolled. The study was approved by Ethics Committee, and written informed consent was obtained from the patients or their relatives. Serum inhibin B concentration were measured spectrophotometrically by using a commercial assay kit, according to the manufacturer's instructions. The data were evaluated with SPSS packed programme (version 17.0 software, SPSS Inc. Chicago, Illinois, USA). Serum FSH, LH, E2, TSH and progesteron concentrations were measured by using Siemens enzyme immunometric assay kit on the ADVIA centeaur CP analyzer in the hospital's biochemistry laboratory.

RESULTS:

Serum Inhibin B concentration were significantly increased in unexplained infertility patients (61.14±43.30 pg/mL) as compared to controls (46.88±8.20 pg/mL) ($p<0.05$). The Inhibin B level was found to significantly correlate with LH/FSH ratio ($r=0.222$, $p<0.05$). It was also correlated with quetelet index positively ($r=0.270$, $p<0.05$), while there were no correlation between inhibin B and others endocrine parameters in patients with unexplained infertility ($p>0.05$). There was no statistically significant difference between patient and control group in terms of age, quetelet index, E2, TSH and progesterone concentrations. On the other hand, there was a significant difference in terms of FSH and LH in two groups ($p<0.05$).

CONCLUSIONS:

Serum Inhibin B levels in unexplained infertility were significantly differ from control group, while these values were in normal range in both groups. Thus, it can be useful for evaluating unexplained infertility. Further studies are warranted to confirm this finding, especially with a larger population.

ACKNOWLEDGEMENTS:

This study was supported by GAZI University Projects of Scientific Investigation (GÜBAP) (Project No : 02/2015-03)

REFERENCES:

1. Missmer SA, Abusief ME, Barbieri RL and Goldman MB (2013). Women and Health (Second Edition), Chapter 17, United States of America, pp 251-270.
2. Broekmans FJ. et al. (2009). Endocr Rev. 30:465–493.

P-399: SERUM CARBONIC ANHYDRASE 1 AND TOS LEVELS IN PATIENTS WITH UNEXPLAINED INFERTILITY

[1] Taskan, T., [1] Turan, T., [2] Pekel, A., [2] Iltemir Duvan, CZ., [1] Gonenc, A.

[1] Gazi University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey

[2] Medical Park Ankara Hospital, Female Obstetrics And Gynecology Clinic, Ankara, Turkey

INTRODUCTION:

Unexplained infertility refers to a diagnosis made in couples in which all the standard examinations, which are usually seen in about 30-40% of infertile couples, are usually normal, such as ovulation, tubal opening, and sperm analysis. One of the possible causes of unexplained infertility have been reported to arise from disorder that occur in productive physiology. Carbonic anhydrase is a zinc enzyme widely found in the living world and has been detected in the human reproductive tract, over, fallopian tube and uterine endometrium. Oxidative stress affects the reproductive system in various stages and free oxygen radicals play a role in several infertility related diseases. Serum Carbonic Anhydrase I (CA I) and TOS values were evaluated for possible association in patients with unexplained infertile patients.

Materials and Method: Our study group, a total of 85 females (age range 18–40 years), including 44 with unexplained infertility and 41 control group. In serum samples CA I levels were measured at 450 nm using an ELISA kit. Total oxidant status (TOS) levels were measured by 530 nm wavelength in a spectrophotometer by manual methods. Measurements were made at Gazi University Faculty of Pharmacy Department of Biochemistry Department. The results were evaluated statistically by SPSS 17.0 package program.

RESULTS:

There was no significant difference in carbonic anhydrase 1 levels between women with unexplained infertility and control group ($p>0.05$). However, we detected TOS levels were statiscally significantly different between the patient and control groups ($p<0.05$).

CONCLUSIONS:

Carbonic anhydrase I concentrations in patiens with unexplained infertility (784.86±56.61) were different from those of controls (752.13±13.10) higher but statiscally not significant. Serum TOS levels in women with unexplained infetility have a lower concentration (6.00±0.16) when compared to controls (6.70±0.31). TOS may have a critical role to unexplained infertility. We hope that this result will applied in larger populations and illuminate the work to be done in the future.

REFERENCES:

1. Ray et al., (2012). Reproductive Bio Medicine, 24:591– 602.
2. Mentese et al., (2013). Turk J Biochem, 38(1):43–48.
3. Palacio et al., (2006). Clinical and Experimental Immunology, 144:217–222.

P-400: ANTIOXIDANT AND ENZYME INHIBITION ACTIVITIES ON DIABETES MELLITUS OF DIFFERENT MOLECULAR WEIGHT CHITOSANS

[1] Cakmak, YS., [1] Kaya, M., [2] Zengin, G.

[1] Department of Biotechnology and Molecular Biology, Faculty of Science and Letters, Aksaray University, Aksaray, Turkey.

[2] Department of Biology, Faculty of Science, Selcuk University, Konya, Turkey.

INTRODUCTION:

Chitosan, a natural biopolymer, has become a remarkable material in recent years due to its positive properties (nontoxic against living organisms, biodegradable, biocompatible, antitumor and antioxidant activity) and its availability in different fields (1-4). The chitosan is obtained with a certain degree deacetylation of chitin for removal of acetyl groups. Some parameters and properties including deacetylation degree, molecular weight, viscosity and solubility determine its using area. Molecular weight has changed with temperature, time and base (NaOH) concentration applied during deacetylation. This study aimed characterization, antioxidant activity and enzyme inhibition of different molecular weights chitosan samples.

MATERIALS AND METHODS:

FT-IR, XRD, TGA and SEM analyzes were used for characterization. For antioxidant activity, DPPH scavenging activity, ferric ion reducing power and FRAP tests were conducted. To determine the diabetes linked enzyme inhibition activities, inhibition of α-amylase and α-glucosidase were investigated.

RESULTS:

The molecular weights of the chitosan deacetylated at 4, 8, 16 and 42 hours were calculated as 1.9, 7.3, 16.9 and 75.1 kDa, respectively. DPPH scavenging and ferric reducing power activities were increased with increasing molecular weight. In other words, when the duration of deacetylation was increased, antioxidant activity was improved. However, there was no relation between the FRAP test and the molecular weight. For both enzymes, increases in the deacetylation time enhanced enzyme inhibition activities. Inhibition activity of α-glucosidase was observed approximately 4 times higher than that of α-amylase.

CONCLUSIONS:

As a result, it was observed that the molecular weight of chitosan positively affected both antioxidant activity and enzyme inhibition. In particular, due to its high inhibition of diabetes-related enzymes, chitosan could be used as a natural alternative to acarbose (a standard substance).

ACKNOWLEDGEMENTS:

This research was supported financially as a project (Project No: 2016/032). We thank to Aksaray University Scientific Research Projects Foundation (ASUBAP) for providing financial support for this study.

REFERENCES:

1. Hutmacher DW (2000). Biomaterials, 21(24):2529-2543.
2. Agnihotri SA, Mallikarjuna NN, Aminabhavi TM (2004). Journal of controlled release, 100(1):5-28.
3. Jayakumar R, Chennazhi KP, Muzzarelli RAA, Tamura H, Nair SV, Selvamurugan N (2010). Carbohydrate Polymers, 79(1):1-8.
4. Sargin I, Arslan G, Kaya M (2016). Carbohydrate Polymers, 138:201-209.

P-401: COMPARISON OF ANTI-INFLAMMATORY ACTIVITIES OF TENOXICAM AND ITS TRANSITION METAL COMPLEXES

[1] Kalaycioglu, Z., [2] Muslu, H., [1] Erim, FB., [1] Golcu, A.

[1] Istanbul Technical University, Faculty of Science and Letters, Department of Chemistry, Istanbul, Turkey

[2] Kahramanmaras Sutcu Imam University, Faculty of Science and Letters, Department of Chemistry, Kahramanmaras, Turkey

INTRODUCTION:

Nonsteroidal anti-inflammatory drugs (NSAIDs) are one of the most important therapeutic agents used for the treatment of a variety of inflammation. Tenoxicam, which is used to relieve inflammation, swelling, and pain associated with rheumatoid arthritis, is a member of NSAIDs. In this study, the effect of metal complexation of tenoxicam on the anti-inflammatory activity was searched.

MATERIALS AND METHODS:

The inhibition of pro-inflammatory cytokine namely tumor necrosis factor-α (TNF-α) is one of the most common approach in the treatment of inflammatory (1).

The serum levels of TNF-α of tenoxicam and Pd, Pt, Zn, and Cu complexes of tenoxicam were determined by in vitro enzyme linked immunosorbent assay (ELISA) kit (Thermo Fisher Scientific, Waltham, MA). Measurements were carried out on a 96-well microplate reader.

RESULTS:

The results were given as the inhibition of TNF-α in percent (I %). Metal complexes of tenoxicam inhibited the TNF-α between 50.6% and 93.6% whereas the TNF-α inhibition of tenoxicam was 47.3%. It means that the anti-inflammatory effects of the metal complexes of tenoxicam are higher than that of tenoxicam. The highest TNF-α inhibition rate was performed by Cu complex (93.6%) which showed comparable bioactivity with the standard drug used (96.3%).

Conclusions:The complexation with metal ions was considerably enhanced the anti-inflammatory activity of tenoxicam which offers a potential application for pharmaceutical industry.

REFERENCES:

1. Beutler B, Cerami A (1989). Annual Review of Immunology 7:625–655.

P-402: SYNTHESIS AND EVALUATION OF NEW BENZAZOLE DERIVATIVES AS POTENTIAL ANTICANDIDAL AGENTS.

[1] Ozdemir, A., [1] Altintop, MD., [1] Sever, B.

[1] Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskisehir, Turkey

INTRODUCTION:

Azoles are by far the most widely used class of antifungal agents. They show their antifungal activity via the inhibition of cytochrome P450-dependent enzyme 14α-lanosterol demethylase (CYP51) (1). Due to the importance of azoles in the field of antifungal drug design, we aimed to design and synthesize new benzazole anticandidal agents.

MATERIALS AND METHODS:

New 1-[5-(1,3-benzodioxol-5-yl)-3-(thiophen-2-yl)-4,5-dihydro-1H-pyrazol-1-yl]-2-[(nonsubstituted/5-substituted-1H-benzazol-2-yl)thio]ethan-1-one (1–8) were synthesized via the reaction of 1-[5-(1,3-benzodioxol-5-yl)-3-(thiophen-2-yl)-4,5-dihydro-1H-pyrazol-1-yl]-2-chloroethan-1-one with aryl thiols. These compounds were evaluated for their in vitro antifungal effects on Candida albicans, Candida glabrata, Candida parapsilosis and Candida krusei. Their minimum inhibitory concentration (MIC, µg/mL) values were determined by a broth microdilution assay. Docking studies were also carried out to predict the affinity of the most effective anticandidal agents to the active site of CYP51 (PDB code: 5JLC) using Schrodinger's Maestro molecular modeling package (Schrödinger Release 2016-2: Schrödinger, LLC, New York, NY, USA). In silico ADME properties of all compounds were determined using Molinspiration software (2).

RESULTS:

Compounds 2, 4 and 6 showed selective antifungal activity against C. albicans with a MIC value of 62.5 µg/mL when compared with ketoconazole (MIC= 62.5 µg/mL). Docking results indicated that chloro substituted compounds 2 and 6 formed cation-π with the iron of Heme group in the active site of CYP51. According to in silico ADME studies, compound 2 only violated one parameter of Lipinski's rule of five making it a potential orally bioavailable agent.

CONCLUSIONS:

According to in vitro and in silico studies, compound 2 stands out as a promising orally bioavailable anticandidal drug candidate for further studies.

REFERENCES:

1. Chen ZF, Ying GG (2015). Environment International, 84:142-153.
2. http://www.molinspiration.com. (Accessed August 2017).

P-403: SYNTHESIS, IN VITRO AND IN SILICO STUDIES OF NEW PYRAZOLINE DERIVATIVES AS POTENTIAL ANTICANDIDAL AGENTS.

[1] Ozdemir, A., [1] Altintop, MD., [1] Sever, B.

[1] Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskisehir, Turkey

INTRODUCTION:

Pyrazolines have attracted a great deal of interest in medicinal chemistry related to their diverse biological activities. In particular, recent studies have indicated that antimicrobial activity of pyrazolines was observed predominantly (1). For this purpose, herein we designed and synthesized new pyrazoline-based anticandidal agents.

MATERIALS AND METHODS:

New 1-[(aryl)thioacetyl]-3-(2-thienyl)-5-(1,3-benzodioxol-5-yl)-2-pyrazolines (1–6) were synthesized via the reaction of 1-(chloroacetyl)-3-(2-thienyl)-5-(1,3-benzodioxol-5-yl)-2-pyrazoline with aryl thiols. In vitro antifungal effects of these compounds were evaluated on Candida albicans, Candida glabrata, Candida parapsilosis and Candida krusei. Their minimum inhibitory concentration (MIC, µg/mL) values were determined by a broth microdilution assay. Molecular docking simulation was performed for compound 5 in the active site of lanosterol 14α-demethylase enzyme (CYP51) (PDB code: 5JLC) using Schrodinger's Maestro molecular modeling package (Schrödinger Release 2016-2: Schrödinger, LLC, New York, NY, USA). Molinspiration software was used for in silico pharmacokinetic evaluation of all compounds (2).

RESULTS:

Compound 5, methyl substituted tetrazole-based agent, revealed high antifungal effect on C. albicans with a MIC value of 62.5 µg/mL when compared with ketoconazole (MIC= 62.5 µg/mL). Docking resuts indicated that the thiophene and the thioacetyl groups of compound 5 presented π-π interaction and H-bond with Phe385, His406 and Tyr73 residues, respectively. Besides the methyltetrazole moiety of this compound also formed π-π interaction and H-bond with His382 and Ser383 residues, respectively. These docking results emphasized that compound 5 might show its anticandidal activity via the inhibition of ergosterol biosynthesis. Therefore, this study must be supported with further in vitro enzyme studies. According to in silico ADME studies, compound 5 did not violate Lipinski's rule making it a potential orally bioavailable anticandidal agent.

CONCLUSIONS:

Compound 5 was identified as a promising anticandidal agent for further mechanistic studies.

REFERENCES:

1. Shaaban MR, Mayhoub AS, Farag AM (2012). Expert Opinion on Therapeutic Patents, 22:253-291.
2. http://www.molinspiration.com. (Accessed August 2017).

P-404: SYNTHESIS AND E/Z SEPARATION OF NEW NAPHTHYL ETHANONE OXIME ESTER DERIVATIVES BEARING PYRAZOLE MOIETY

Bozbey, I., Karakurt, A.

Inonu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Malatya, Turkey

INTRODUCTION:

Isomerism finds its importance in the area of medicinal chemistry, as isomers differ in their pharmacokinetic and pharmacodynamic properties. Drug isomerism has opened a new field for drug development (1). Oximes also show geometric isomerism because they carry carbon-nitrogen double bonds. The geometric isomers E and Z of oxime and oxime esters are important since their physical, chemical, steric properties are different. There are different activities among the isomers. The oxime isomers should be considered as two different substances because of their properties (2-4). From this point of view, in the present study some aryl ethanone oxime derivatives bearing pyrazole moieties were designed, synthesized and separated.

MATERIALS AND METHODS:

We synthesized compounds by the reaction of oxime derivate (d) with various acyl chlorides using Nao. The compounds were separated E/Z isomer by using several solvents. Their structures were confirmed by IR, 1H-NMR, 13C-NMR and elemental analysis data.

RESULTS:

Compounds were obtained as E and Z isomer. E/Z structure was determined by 1H-NMR. Melting point and Rf values were detected.

CONCLUSIONS:

E/Z isomers with different configurations have different physicochemical and pharmacological properties and pharmacological activities. Thus, we obtained the compounds separately as E and Z and evaluated their pharmacological activities separately.

ACKNOWLEDGEMENTS:

This study was supported by a grant of INU-BAP (2011/65)

REFERENCES:

1. M. Nabil Aboul Enein et al., (1998). ilFarmaco, 53:197-208.
2. Jerslev B (1957). Crystal Structure of Oximes. Nature, 180:1410-1412.
3. Tegyey Z, Matkovics B (1968). Magy. Kem. Foly., 74 (3):116-119.
4. Haney WG et al., (1977). J Pharm Sci, 66(11):1602-1606.

P-405: MOLECULAR DOCKING STUDIES ON NEW 1-(4-TRIFLOUROMETHYL)PHENYL-2-(1H-IMIDAZOL-1-YL)ETHANONE OXIME ESTER COMPOUNDS

[1] Bozbey, I., [1] Uslu, H., [1] Karakurt, A.

[1] Inonu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Malatya, Turkey

INTRODUCTION:

The incidence of fungal infections, which became a serious threat to human health, has increased in recent years. Especially, systemic mycoses have higher morbidity and mortality rates in conditions that suppress the immune system such as patients with AIDS, cancer patients. It is an infectious disease that is often acquired at the hospital. Candida species are main cause of mycoses in humans. Invasive candidiasis with a high mortality rate is the most frequently isolated C.albicans. However, infections caused by other candida species are increasing recently (1,2). In this study, we have investigated the interactions between new oxime ester compounds and active enzyme sites.

MATERIALS AND METHODS:

Structure of synthesized compound were determined by spectral and elemental analyses. “Structure of CYP51 from the pathogen Candida albicans” pdb file with resolution 2.9Å (PDB ID:5v5z) was received (www.rcsb.org) and was modified using the ADT package version 1.5.6rc3. To validate the docking program, the co-crystallized ligand Itraconazole (PDB ID:1YN) was redocked on the target enzyme and RMSD value of 1.846 was found for Itraconazole-bound CYP51. RMSD value was obtained using Lamarckian Genetic Algorithm and scoring function of AutoDock 4.2 release 4.2.5.1 software (3).

RESULTS:

In order to rationalize their mechanism of action, we performed computational analysis utilizing molecular docking on the C.albicans CYP51 homology models we built. 4a occupied van der Waals interactions with Tyr118, Thr122, Phe126, Phe228, Gly307, Thr311, Leu376, Ser378, Phe380, Met508, HEM. 4b occupied van der Waals interactions with Tyr118, Thr122, Phe126, Phe228, Phe233, Gly307, Thr311, Leu376, Ser378, Phe380, Met508, HEM.

CONCLUSIONS:

Docking studies were performed for the most active compounds. As a result of these studies, a strong interaction between these compounds and the active sites of enzyme was revealed.

ACKNOWLEDGEMENTS:

This study was supported by a grant of INU-BAP (2017/803)

REFERENCES:

1. Silva S et al., (2012). Fems Microbiol Rev. 36(2):288-305.
2. Wong SSW, Samaranayake LP, Seneviratne CJ (2014). Drug Discov Today. 19(11):1721-30.
3. Morris GM et al., (2009). J. Computational Chemistry. 16:2785-91.

P-406: RESTRICTED ROTATION AROUND THE METHYLENE BRIDGE OF 5-(2-P-(CHLOROPHENYL)BENZIMIDAZOLE-1-YL)METHYL-4-(O SUBSTITUTEDPHENYL)-2,4-DIHYDRO-[1,2,4]-TRIAZOLE-3-THIONES AS EVIDENCED BY NMR, X-RAY AND DFT STUDIES

[1] Karayel, A., [2] Ozbey, S., [3] Kus, C., [3] Ayhan Kilcigil, G.

[1] Hitit University, Department of Physics, Corum, Turkey

[2] Hacettepe University, Physics Engineering Department, Ankara, Turkey

[3] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry Ankara, Turkey

INTRODUCTION:

Benzimidazoles have become an important pharmacophore in drug design and have been screened for a wide range of biological activities e.g. antimicrobial (1), antiparasitic (2), antihistaminic (3), anticancer (4), and antioxidant (5). The aim of this study was to clarify the restricted rotation around the –CH2-N bond of the compounds, 5-(2-(p-chlorophenylbenzimidazol-1-yl-methyl)-4-(o-methylphenyl)-2,4-dihydro-[1,2,4]-triazole-3 thione (1), 4-(o-florophenyl)- (2), 4-(o-chlorophenyl)- (3) and 4-(o-bromophenyl)- (4), which are some benzimidazole derivatives showing antioxidant properties, as a comparatively the experimental results (NMR and X-ray) with DFT. We also present here the crystal, and molecular structure of the compound 3 and 4 with the X-ray diffraction method.

MATERIALS AND METHODS:

Solid state geometry was determined in order to see intra- and inter-molecular interactions by X-Ray. We determined by the NMR experiments whether the effect of temperature and solvents on the rotation barrier. The geometric and conformational parameters of the molecules were investigated with DFT.

RESULTS:

In NMR spectra of relevant compounds, because of the hindered rotation around the methylene bridge, methylene protons appear as an AB quartet in DMSO-d6. The high temperature NMR spectra for the compound 1 show similar behavior in DMSO-d6. The NMR spectra in different solvents point out the same manner. The preventing of free rotation in the methylene bridge caused by the existence of substituents at the second position of the phenyl group connected to triazole ring was supported by both the experimental results (NMR and X-ray) and the theoretical results.

CONCLUSIONS:

The single crystal X-ray structures of these compounds show the presence of the strong intra-molecular interaction and close contact, preventing of free rotation in the methylene bridge. Also, DFT scans of the relevant compounds are in line with hindering of rotation.

REFERENCES:

1. Goker H, Alp M, Ates Alagoz Z, Yildiz S (2009). J Heterocyclic Chem., 46:936–948.
2. Alp M, Goker H, Brun R, Yildiz S (2009). Eur J Med Chem., 44:2002–2008.
3. Goker H, Ayhan Kilcigil G, Tuncbilek M et al.(1999). Heterocycles, 51:2561–2573.
4. Cheong JE, Zaffagni M, Chung I et al. (2018) .Eur J Med Chem., 144:372-385,
5. Can-Eke B, Puskullu MO et al. (1998). Chem-Biol Interact., 113:65-77.

P-407: SYNTHESIS OF NOVEL N-NAPHTHALENE-2-YL PROPANAMID DERIVATIVES AND EVALUATION THEIR ANTIMICROBIAL ACTIVITY

[1] Evren, AE., [1] Yurttas, L., [2] Yilmaz Cankilic, M.

[1]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Anadolu University, Eskisehir, Turkey.

[2]Department of Biology, Faculty of Sciences, Anadolu University, Eskisehir, Turkey.

INTRODUCTION:

Pathogenic organisms cause of the communicable or infectious diseases may be classified by size as microscopic organisms, macroscopic organisms and microscopic particles. Bacterial and fungal (microscopic organisms) infections are sort of highly prevalent diseases. Since the first report about antimicrobial resistance in 1940's, researchers have discovered the new, safer and efficient antimicrobial agents has been became required (1, 2). Among various aromatic compounds, naphthalene

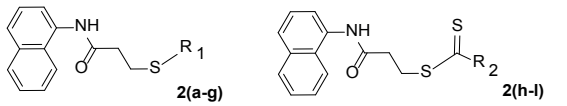
derivatives have displayed very different biological activities. Especially, their anticancer, antifungal and antibacterial activities (3, 4) drew our attention. By the reason of the above information, we synthesized new twelve N-(naphthalene-2-yl)propanamide derivatives as potential antimicrobial agent.

MATERIALS AND METHODS:

The synthesis reaction was carried out via two steps. After amidation reaction, the obtained product (1) was separated to two pieces. One of these pieces was reacted with 2-mercapto azole derivatives. The other of them was reacted with dithiocarbamate salts attached to different heterocyclic amines. MIC values of final compounds (2a-2l) were determined against ten fungi and ten bacteria.

RESULTS AND DISCUSSION:

All compounds (2a-2l) have shown an antimicrobial activity. Especially 2a, 2b, 2c, 2e and 2f have demonstrated high activity against Staphylococcus aureus (ATCC 6538), Yersinia enterocolitica (Y53), Candida albicans (ATCC 90028) and Candida krusei (ATCC 6258).



R_1: $-C_3H_3N_2S$, $-C_7H_4NS$, $-C_4H_5N_2$, $-C_8H_7N_2O$, $-C_7H_4N_3O_2$, $-C_3H_4N_3$ $-C_6H_5$
R_2: $-C_5H_{10}N$, C_4H_8NO, $C_8H_{11}N_4$, $-C_{11}H_{15}N_2$, $-C_{10}H_{13}N_2$

CONCLUSIONS:

Be specified due to results, 2-mercopta azole derivatives' activities are better than dithiocarbamate salt derivatives' activity.

REFERENCES

1. Shih RY,Koeller KK (2015). Radiographics, 35:1141-1169.
2. Evren AE, Tekinkoca S,Yurttas L (2017). Lett Drug Des Discov, 14:154-159.
3. Kabir MS, Namjoshi OA, Verma R, Polanowski R, Krueger SM, Sherman D, Rott MA, Schwan WR, Monte A,Cook JM (2010). Bioorg Med Chem, 18:4178-4186.
4. Tandon VK, Maurya HK, Mishra NN,Shukla PK (2009). Eur J Med Chem, 44:3130-3137.

P-408: DESIGN, SYNTHESIS AND ANTIMICROBIAL ACTIVITIES OF TRIAZOLE DERIVATIVES

[1] Kubilay, A., [1] Evren, EA., [1] Yurttas, L., [2] Kisacik, I., [2] Gencer Karaca, H.

[1] Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskişehir, Turkey

[2] Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Eskişehir, Turkey

INTRODUCTION:

Microbial infections cause millions of people to die each year due to lack of effective treatment and microbial resistance to antibiotics. The formation of antibiotic resistance pathogens has become a serious health problem, and a number of studies have been conducted to improve existing antimicrobial treatments (1). In researches, the biological activities of heterocyclic ring-containing compounds are also remarkable. Triazoles have attracted interest because they exhibits a large number of biological activities such as antimicrobial, analgesic, anti-inflammatory, anticancer, antioxidant (2,3). In this work, the synthesis of some new 3,4,5-trisubstituted triazole derivatives, spectroscopic methods of structure elucidation and evaluation of antimicrobial activities of compounds are aimed.

MATERIALS AND METHODS:

8-Hydroxyquinoline and ethyl chloroacetate were mixed by boiling. After reaction is completed, the solvent was evaporated and the material was washed with water to acquire the intermediate. The obtained product, ethyl 2-(quinolin-8-yloxy)acetate (1) was reacted with hydrazine hydrate in ethanol. At the end of the reaction, hydrazinated compounds was gained by filtration. 2-(Quinolin-8-yloxy)acetohydrazide (2) was dissolved in ethanol and boiled with phenylisothiocyanate to synthesize N-phenyl-2-(2-(quinolin-8-yloxy)acetyl)hydrazine-1-carbothioamide (3) and then in next step this compound was refluxed with 2N potassium hydroxide prepared in ethanol. The reaction was terminated by controlling the TLC. The pH was set to 7 to allow the material to settle in a cold environment. At last, the resulting triazole molecule (4) was treated with appropriate 2-chloro-N-substitute acetamide derivates to get final twelve derivatives (5a-l). The antimicrobial activity of the compounds was screened on eight bacteria and three fungi. Fluconazole and chloramphenicol were used as standard drugs. Minumum inhibitor concentrations (MIC) were determined for each compound and standards.

RESULTS:

The aimed twelve compounds (5a-l) were obtained purely and the structures of the compounds were elucidated with spectroscopic methods. The activities of the compounds against Salmonella and Candida species have been determined higher and comparable to standards.

CONCLUSIONS:

Compounds 5a bearing 6-nitrobenzothiazole and 5k bearing 2-acetyl-3-methyl thiazole showed the highest antibacterial activity at 7.8, 7.8 µg/ml, respectively.

REFERENCES:

1. Allahverdiyev AM, Abamor ES, Bagirova M, Rafailovich M (2011). Future Microbiol, 6:933-940.
2. M.Isloor A, Kalluraya B, Shetty P (2009). European Journal of Medicinal Chemistry, 44:3784-3787.
3. Tozkoparan B, Gokhan N, Aktay G, Yesilada E, Ertan M (2000). European Journal of Medicinal Chemistry, 35:743-750.

P-409: INDOLE-BASED MELATONINE ANALOGUES AS POTENT INHIBITOR OF ROS

[1] Yilmaz, AD., [2] Coban, T., 1 Suzen, S.

[1]Ankara University Faculty of Pharmacy, Pharmaceutical Chemistry Department, Ankara, Turkey

[2]Ankara University Faculty of Pharmacy, Pharmaceutical Toxicology Department, Ankara, Turkey

INTRODUCTION:

Melatonin is a direct scavenger of free radicals, which is associated to its ability to protect cells from oxidative stress (1, 2). We have revealed from our previous research that MLT-related compounds exhibit good antioxidant activity in vitro (3,4).

MATERIALS AND METHODS:

In this study 5-chloroindole hydrazide/hydrazone derivatives which was synthesized from 5-chloroindole-3-carboxaldehyde and various phenyl hydrazine derivatives. All synthesized compounds characterized and in vitro antioxidant activity was investigated against MLT and BHT.

RESULTS:

Most of the compounds showed strong inhibitory effect on the superoxide radical scavenging assay at 1 mM concentration (79 to 95%). Almost all the tested compounds possessed strong scavenging activity against the DPPH radical scavenging activity with IC50 values (2 to 60 µM).

CONCLUSIONS:

These results found promising for further research on melatonin analogue compounds.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (109S099)

REFERENCES:

1. Antunes F, Ross L, Barclay C, Ingold KU, Kıng M, Norrıs JQ, Scaıano JC, XI, F (1999). Free Rad. Biol. Med., 26:117-128.
2. Gupta, YK, Gupta M, Kohlı K (2003). Indian J. Physiol. Pharmacol., 47:373-386.
3. Ates Alagoz Z, Coban T, Suzen S (2005). Med. Chem. Res., 14(3)169-179.
4. Suzen S, Ates-Alagoz Z, Demırcıgıl T, Ozkan SA (2001). Il Farmaco 56:835-840.

P-410: SYNTHESIS AND CYTOTOXIC ACTIVITIES OF NOVEL CHIRAL SULFONAMIDES AS HYPOXIA INDUCED FACTORS INHIBITORS

[1] Karakucuk Iyidogan, A., [2] Bayram, H., [3] Tasdemir Kahraman, D., [4] Saygideger Kont, Y., [1] Taskin Tok, T., [1] Basaran, E., [3] Ilhan, S., [1] Oruc Emre, EE.

[1]Gaziantep University, Faculty of Art and Sciences, Department of Chemistry, Gaziantep, Turkey

[2]Koc University, Faculty of Medicine, Department of Pulmonary, Istanbul, Turkey

[3]Gaziantep University, Faculty of Medicine, Laboratory of Cell Culture, Gaziantep, Turkey

4Cukurova University, Faculty of Medicine, Department of Pulmonary Adana, Turkey

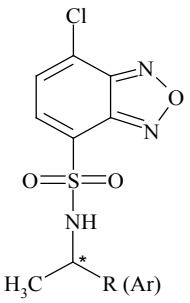
INTRODUCTION:

Hypoxia is a common occurrence in solid tumors largely due to inadequate vascularization, which eventually leads to the development of tumor necrosis. Hypoxic conditions are well known to hinder the effectiveness of chemotherapy and radiation therapy. HIF-1 activity in tumors depends on availability of the HIF-1α subunit, the levels of which increase under hypoxic conditions and through activation of oncogenes and/or inactivation of tumor suppressor genes (1-3). In this work, the novel compounds bearing benzoxadiazole and chiral sulfonamide moieties on the same molecule were designed and synthesized.

MATERIALS AND METHODS:

The chemical structures of the synthesized compounds were confirmed by elemental analysis, IR, 1H NMR, 13C NMR, and mass spectral data. Their possible in vitro cytotoxic activities against broncho-alveolar carcinoma cell line (A549) were evaluated and cell viability was assessed using MTT assay at

the hypoxia and normoxia conditions. Additionally, interaction mechanisms among these compounds and HIF-1α at the molecular level were identified by in silico studies.



RESULTS:

Higher concentrations (225μM) of 2a and 7a ($p<0.05$), 1a, 1b, 4b, 6a and 7b ($p<0.01$), 2b, 3b, 5a, 5b and 6b ($p<0.001$) were significantly decreased in normoxia condition on A549 cell viability after 24 hours. Similarly, for hypoxia conditions; higher concentrations (225μM) of 1a, 1b and 7b ($p<0.001$) were significantly decreased A549 cell viability after 24 hours. 75 μM of compounds 3b, 4b, 6a, 6b and 7a ($p<0.01$) significantly decreased A549 cell viability as compared to controls.

CONCLUSIONS:

These findings demonstrated that the novel sulphonamide derivatives exhibited cytotoxic activity against A549 cell line under hypoxia and normoxia conditions.

ACKNOWLEDGEMENTS:

This work supported by TUBITAK with the project number 114Z960.

REFERENCES:

1. Vaupel P, Mayer A (2007). Cancer Metastasis Review, 26:225-39.
2. Burroughs SK, Kaluz S et al., (2013). Future Medicinal Chemistry, 5:553-72.
3. Tan C., De Noronha RG et al., (2011). Bioorganic. Medicinal Chemistry Letters, 21:5528-32.

P-411: SYNTHESIS AND BIOLOGICAL EVALUATION OF 3-[(4-SUBSTITUTED-1-YL) PHENYL]-1-ARYL/HETEROARYL-2-PROPEN-1-ONE DERIVATIVES

[1] Karakucuk Iyidogan, A., [2] Sicak, Y., [1] Kakaj Mohamad, H., [3] Ozturk, M., [1] Oruc Emre, EE.

[1]Gaziantep University, Faculty of Art and Sciences, Department of Chemistry Gaziantep, Turkey

[2]Mugla Sıtkı Kocman University, Koycegiz Vocational School, Department of Aromatic and Medicinal Plants, Mugla Turkey

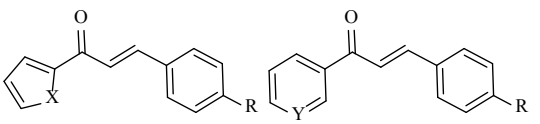
[3]Mugla Sıtkı Kocman University, Faculty of Sciences, Department of Chemistry, Mugla Turkey

INTRODUCTION:

1,3-diphenyl-2-propen-1-ones are named as chalcones, α,β-unsaturated ketone compounds which belong to the flavonoid family. Chalcones and their heterocyclic derivatives have been known to possess many pharmacological activity such as anticancer, antiinflammatory, antimicrobial, antioxidant, antimalarial, antileishmanial, antiulcer, antiviral, antiprotozoal and anti-HIV (1-3).

MATERIALS AND METHODS:

In the present work, the new chalcones with potential biological activity were synthesized. 3-[(4-substituted-1-yl)phenyl]-1-aryl/heteroaryl-2-propen-1-one derivatives (1a-d, 2a-d, 3a-d, 4a-d and 5a-d) were synthesized starting from 4-substituted-benzaldehydes and aromatic/heteroaromatic methyl ketones by Claisen-Schmidt condensation reaction (4). The chemical structures of chalcone derivatives were eludicated by FT IR, 1H NMR, 13C NMR and MS spectral data and Elemental analyses (CHNS).



X: O, S, NH Y: CH_2, N

R: morpholino, piperidine, pyrrolidine, imidazolyl, pyrimidine

RESULTS:

The antioxidant activity of 3-[(4-substituted-1-yl) phenyl]-1-aryl/heteroaryl-2-propen-1-one derivatives was determined as β-carotene-linoleic acid, DPPH radical scavenging, superoxide anion radical scavenging, ABTS cation radical scavenging, and CUPRAC methods. In vitro inhibitory activity of acetylcholinesterase and butyrylcholinesterase enzymes related with Alzheimer's disease was determined using Ellman's method (5).

CONCLUSIONS:

Compound 1, 2 and 5 series may be used as pharmaceutical agents for antioxidant. 1, 2 and 5 series were found to be active against AChE. We conclude that all synthesized compounds can be considered as a candidate for BChE inhibitor.

ACKNOWLEDGEMENTS:

This study is supported by the Gaziantep University Scientific Research Projects Governing Unit with the project number FEF.YLT.17.17.

REFERENCES:

1. Deng J, Sanchez T, et al., (2007). Bioorganic Medicinal Chemistry, 15:4985-5002.
2. Romagnoli R, Baraldi, PG, et al., (2008). Letters in Drug Design Discovery, 5:214-220.
3. Fu DJ, Zhang SY, et al., (2016). Journal of Chemical Research, 40:620-623.

4. Kursun Aktar BS, Oruç-Emre EE, et al., (2017). Journal of Molecular Structure, 1149:632-639.
5. Ellman GL, Courtney KD, et al., (1961). Biochemistry and Pharmacology and Behaivor, 7:88-95.

P-412: IN VITRO ANTI-INFLAMMATORY ACTIVITY OF NOVEL 5-FLUORO AND 5-METHOXY INDOLE-PIPERAZINE DERIVATIVES

[1] Altuntas, TG., [1] Baydar, A., [2] Yilmaz, S., [2] Coban, T.

[1] Ankara University, Department of Pharmaceutical Chemistry, Ankara, Turkey

[2] Ankara University, Department of Pharmaceutical Toxicology, Ankara, Turkey

INTRODUCTION:

The generation of oxygen free radicals is known to be involved in the development of the inflammatory process. These radicals are highly reactive molecules with an unpaired electron and can damage or destroy the normal function of a living cell, and allow for the development of many different diseases, including inflammation, cancer, diabetes, cardiovascular, neurodegenerative and pulmonary diseases (1). Finding novel anti-inflammatory agents are important. Indole structure seems to protect body against inflammation and oxidative stress.

MATERIALS AND METHODS:

In this study, the membrane stabilizing activity of the compounds was evaluated by using heat induced human erythrocyte hemolysis. Fresh whole human blood was collected from healthy human volunteer. The tubes were centrifuged at 3000 rpm for 10 min and then the packed cells were washed with isotonic saline. All the centrifuge tubes containing reaction mixture were incubated at 56ºC for 30 min. Then the tubes were cooled and centrifuged at 2500 rpm for 5 min. The absorbance of the supernatant was measured at 560nm. The experiment was performed in triplicates for all the test samples The results were expressed as IC_{50}(2).

RESULTS:

In this study, all the synthesized compounds were tested to evaluate the red blood cell membrane stabilizing effect as an indicator of anti-inflammatory activity. Compound A-11 demonstrated the strongest membrane stabilizing effect (IC50:0,33mM) among the other compound followed by A-10 and A-05 respectively.

CONCLUSIONS:

Our study showed that some of the newly synthesized compounds possess anti-inflammatory properties.

REFERENCES:

1. Reuter S, Gupta SC, Chaturvedi MM, Aggarwal BB (2010). Free Radic Biol Med., 49:1603–1616.
2. Debnath PC, Das A, Sajib AI, Hassan MM. Pharmacognosy Journal, 2013. 5:104-107.

P-413: SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF AMIDE, SULFONAMIDE AND THIOUREA DERIVATIVES BEARING 1,3-OXAZOLIDINONES

[1] Karaman, N., [1] Karakucuk Iyidogan, A., 2 Kocyigit Kaymakcioglu, B., [3] Kapkac, HA., [4] Karaca Gencer, H., [5] Ilgin, S., [5] Karaduman, B., [1] Zainel, RA., [1] Oruc Emre, EE.

[1]Gaziantep University, Faculty of Arts and Sciences, Department of Chemistry, Gaziantep, Turkey.

[2]Marmara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, İstanbul, Turkey.

[3]Anadolu University, Faculty of Science, Department of Biology, Eskisehir, Turkey.

4Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology,Eskisehir, Turkey.

5Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Eskisehir, Turkey.

INTRODUCTION:

1,3-Oxazolidine-2-one is an important heterocyclic ring participating in chemical structure of many drugs. In this research, new 1,3-oxazolidin-2-one derivatives were designed and synthesized in order to be used in the treatment of infections caused by gram positive bacteria's which were resistant to different antibiotics (1-3).

MATERIALS AND METHODS:

The twenty two new amide/sulfonamide/thiourea derivatives were obtained by the reaction of (S)-4-(4-aminobenzyl)-2(1H)-1,3-oxazolidinone with 4-substituted benzoyl chlorides/4-substitutedbenzene sulfonyl chlorides and 4-substitutedphenyl isothiocyanates (4). The structures of all synthesized compounds were clarified by FTIR, NMR, mass spectroscopic data and elemental analysis. All compounds were screened for their antimicrobial activity. Antimicrobial susceptibility and cellular physiology were evaluated using Microbroth dilution assay and flow cytometry method.

RESULTS:

As a result, it was determined that compound 16 displayed better antimicrobial activity than chloramphenicol aganists gram positive bacteria especially Staphylocuccus aures. In addition, genotoxicity, cytotoxicity and ADME parameters of compound 16 was examined and it was found as non-

mutagenic and non-cytotoxic at the concentration it showed antimicrobial activity.

CONCLUSIONS:

According to calculated ADME parameters and drug likeness scores, the compounds can be good drug candidates especially compound 16.

REFERENCES:

1. Balasubramanian V, Solapure S et al., (2014). Antimicrobial Agents Chemotherapy, 58:495-502.
2. Diekema DJ, Jones RN (2001). The Lancet, 358:1975-1982.
3. Gordeev MF, Yuan ZY (2014). Journal of Medicinal Chemistry, 57:4487-4497.
4. Kocyigit-Kaymakcioglu B, Toklu HZ et al., (2008). Journal of Enzyme Inhibition and Medicinal Chemistry, 23:454-461.
5. Karaca Gencer H, Cevik UA et al., (2017). Molecules, 22:507.

P-414: SYNTHESIS OF SOME NOVEL THIOUREAS DERIVATED FROM 4-METHYLBENZENE-1-SULFONAMIDE

[1] Karakucuk Iyidogan, A., 2 Kocyigit Kaymakcioglu, B., [1] Demircan, B., [1] Fusseini A., [1] Oruc Emre, EE.

[1]Gaziantep University, Faculty of Arts and Sciences, Department of Chemistry, Gaziantep, Turkey

[2]Marmara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, İstanbul, Turkey

INTRODUCTION:

During recent years there have been intense investigations on the different classes of thiourea compounds. N,N'-Disubstituted thioureas belong to biologically highly active skeletons. Various thiourea derivatives were extensively studied for their anticancer, antitubercular, antiviral, antifungal, antibacterial, anti-HIV, antihypertensive, anticonvulsants activities. In this research, sulfonylthiourea derivatives were synthesized with the aim of new pharmalogical drug development (1-3).

MATERIALS AND METHODS:

A series of new sulfonylthiourea derivatives (4-methyl-N-[(4-substitutedphenyl)carbamothioyl]benzene-1-sulfonamides) were obtained by the condensation of 4-methylbenzene-1-sulfonamide with appropriate isothiocyanates in prensence of K2CO3 (4). The chemical structures of the synthesized compounds were illuminated using IR, 1H-NMR, mass spectroscopy and elemental analysis.

RESULTS:

The 1H-NMR spectrum of 4-methylbenzene-1-sulfonamide showed a singlet corresponding to NH2 protons at 7.20 ppm. The disappearance of aniline protons (NH2) and the appearance of thiourea NH at 7.60–8.94 ppm proved the formation of the target molecules. All other protons were detected expected values.

CONCLUSIONS:

The spectral data demonstrated that the compounds were synthesized. The sulfonylthiourea derivatives will be tested their antioxidant activity.

REFERENCES:

1. Faidallah HM, Basaif SA et al., (2002) Phosphorus, Sulfur, and Silicon and the Related Elements, 177:671-683.
2. Zaib S, Saeed A et al., (2014). European Journal of Medicinal Chemistry, 78:140-150.
3. Bashir R, Yaseen S et al., (2012). Medicinal Chemistry Research, 21:428-436.
4. Kocyigit-Kaymakcıoglu B, Aker RG et al., (2011). Medicinal Chemistry Research, 20:607-614.

P-415: SYNTHESIS, ANTIOXIDANT ACTIVITY AND ANTICHOLINESTERASE INHIBITORY ACTIVITY OF SOME NEW PYRAZOLE DERIVATIVES

[1] Sicak, Y., [2] Kursun Aktar, BS., [3] Emre Oruc, EE.,[4] Ozturk, M., [1] Aydogmus Ozturk, F., [5] Demirtas, I., [4] Nademm, S., [4] Ozler, MA., [3] Iyidogan Karakucuk, A.

[1] Mugla Sıtkı Kocman University, Department of Aromatic and Medicinal Plants, Mugla Turkey

[2] Cankırı Karatekin University, Department of Property Protection and Security, Cankırı Turkey

[3] Gaziantep University, Department of Chemistry, Gaziantep Turkey

[4] Muğla Sıtkı Koçman University, Department of Chemistry, Mugla Turkey

[5] Cankırı Karatekin University, Department of Chemistry, Cankırı Turkey

INTRODUCTION:

Pyrazole, which is used clinically applicable,consists of two nitrogen atoms, two unsaturated bonds and 5-membered ring. Pyrazole derivatives have been focused great attention some drugs which posess anti-inflammatory, analgesic and antipyretic activiy, are containing pyrazole ring such as celecoxib, rimonabant, antipyrine and ramifenazone. In this study, new pyrazole derivatives (1-12) were synthesized carrying morpholine ring. The synthesized compounds were screened for their antioxidant activity and anticholinesterase inhibitory activity.

MATERIALS AND METHODS:

New pyrazole derivatives (1-12) synthesized from cyclization of substitued hydrazine with morphonylbenzaldehyde in ethanole (1). The structures of the synthesized compounds were elucidated by spectroscopy methods as FTIR, ^{1}H

NMR, 13C NMR and elemental analysis (C, H, N, S). The antioxidant capacity of the compounds was evaluated by using four complementary tests. The anticholinesterase inhibitor activity test was screened according to the Ellman method (2).

RESULTS:

According to test results β-carotein-lineloic acid, DPPH radical scavenging assay, ABTS cation scavenging assay, and CUPRAC assay compound 11 and 12 exihibited better activity than the other compounds. The anticholinesterase activity was performed against acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) enzymes. Compound 12 (IC50: 30.54 ± 0.45 mM) inhibited BChE better than galantamine (IC50: 56.65 ± 0.27 mM).

CONCLUSIONS:

We conclude that the compound 12 can be considered as a candidate for BChE inhibitor.

ACKNOWLEDGEMENTS:

This study is supported by the Mugla Sıtkı Koçman Research Fund with the project number 15/089.

REFERENCES:

1. Pandey D., Nag AK (2000). Asian Journal of Chemistry, 12, 612-614.
2. Ellman GL, Courtney KD et al., (1961). Biochemistry and Pharmacology and Behaivor, 7: 88-95.

P-416: SYNTHESIS AND BIOLOGICAL ACTIVITIES OF CHIRAL PYRAZOLE DERIVATIVES

[1] Sicak, Y., [2] Kursun Aktar, BS., [3] Emre Oruc, EE., [4] Ozturk, M., [1] Aydogmus Ozturk, F., [5] Demirtas, .I, [4] Nademm, S., [4] Ozler, MA., [3] Iyidogan Karakucuk, A.

[1] Muğla Sıtkı Koçman University, Department of Aromatic and Medicinal Plants, Muğla Turkey

[2] Çankırı Karatekin University, Department of Property Protection and Security, Çankırı Turkey

[3] Gaziantep University, Department of Chemistry, Gaziantep Turkey

[4] Muğla Sıtkı Koçman University, Department of Chemistry, Muğla Turkey

[5] Çankırı Karatekin University, Department of Chemistry, Çankırı Turkey

INTRODUCTION:

Pyrazole and piperidine rings are very commonly used in the medicinal chemistry in the new drug design. Therefore, this study was aimed to synthesize new pyrazole derivatives (1-12) starting piperidinylbenzaldehyde. And also, the synthesized compounds were screened for their antioxidant activity and anticholinesterase inhibitory activity.

MATERIALS AND METHODS:

New pyrazole derivatives (1-12) synthesized from cyclization of substitued hydrazine with piperidinylbenzaldehyde in ethanole (1). The structures of synthesized compounds were elucidated by spectroscopy methods as FTIR, ^{1}H NMR, 13C NMR and elemental analysis (C, H, N, S). The antioxidant capacity of the compounds was evaluated by using four complementary tests. The anticholinesterase inhibitor activity test was screened according to the Ellman method (2).

RESULTS:

The results showed that compound 11 and 12 had the higher lipid peroxidation inhibitory activity than the other compounds. In DPPH radical scavenging assay, compounds 6 and 12 demonstrated better activity than reference standard BHT, while in ABTS cation scavenging assay compound 11 and 12 exhibited better activity among the other compounds. The CUPRAC assay compound 11 and 12 founded better activity among the other compounds. The anticholinesterase activity was performed against acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) enzymes . Compound 12 (IC50: 46.42 ± 0.48 mM) inhibited BChE better than galantamine (IC50: 56.65 ± 0.27 mM).

CONCLUSIONS:

Compound 11 and 12 may be developed as pharmaceutical agents for antioxidant. We conclude that the compound 12 can be considered as a candidate for BChE inhibitor.

ACKNOWLEDGEMENTS:

This study is supported by the Mugla Sıtkı Koçman Research Fund with the project number 15/089.

REFERENCES:

1. Pandey D, Nag AK (2000). Asian Journal of Chemistry, 12, 612-614.
2. Ellman GL, Courtney KD et al., (1961). Biochemistry and Pharmacology and Behaivor, 7: 88-95.

P-417: DETERMINATION OF FREE RADICAL SCAVENGING CAPACITY OF 4,5-DIHYDRO-1H-PYRAZOLE AND HYDRAZONE DERIVATIVES

[1] Evranos Aksoz, B., [2] Yilmaz Sarialtın, S., [2] Coban, T.

[1]Medicines and Medical Devices Agency, Analyses and Control Laboratories, Ankara, Turkey

[2] Ankara University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

INTRODUCTION:

Oxidative damage caused by reactive oxygen species was considered relevant to diseases such as cancer, neurodegenerative diseases, cardiovascular diseases and diabetes. Antioxidants act by clearing or preventing ROS formation, thus protecting against the formation of free radicals and delaying the progress of many chronic diseases including cancer (1). 4,5-Dihydro-1H-pyrazole and hydrazone derivatives have been reported to possess diverse pharmacological activities such as antidepressant, antibacterial, and antioxidant (2, 3). In light of these findings, we synthesized some 4,5-Dihydro-1H-pyrazole and hydrazone derivatives and evaluate them for their antioxidant activities.

MATERIALS AND METHODS:

The total antioxidant activity of compounds was measured by ABTS•+ radical cation decolorization assay (4) using trolox as the standard. The DPPH radical scavenging activities of compounds were examined and compared to known antioxidant BHT, using a reported method by Blois (5).

RESULTS:

Compounds ((5-(4-bromophenyl)-3-(2-hydroxy-4-methoxyphenyl)-4,5-dihydro pyrazol-1-yl)(pyridin-4-yl)methanone) (SH44) and (N'-((E)-1-(4-fluorophenyl)-3-p-tolylallylidene)furan-2-carbohydrazide) (SH37) were found to interact with the stable free radical DPPH•. The most active compound on DPPH• free radical scavenging capacity is SH 44 with IC50 value of 0,50 mM followed by SH37. Similar to the results of this assay, SH 44 demonstrated strong scavenging activity (IC50: 0.06 mM) on ABTS•+ radical, compared to trolox. ((5-(4-methoxyphenyl)-3-(naphthalen-2-yl)-4,5-dihydropyrazol-1-yl)(pyridin-4-yl) methanone) (SH25) showed no effect on both free radicals.

CONCLUSIONS:

2-Hydroxy-4-methoxy phenyl substitution at the third position of pyrazoline ring increased the antioxidant activity.

REFERENCES:

1. Lobo V, Patil A, et al., (2010). Pharmacognosy Reviews, 4(8):118-126.
2. Jagadish PC, Soni N, et al., (2013). Journal of Chemistry, 2013:*1*-6.
3. Ali R, Marella A et al., (2012). Indonesian Journal of Pharmacy, 23(4):193-202.
4. Re R, Pellegrini N et al., (1999). Free Radical Biology Medicine, 26(9-10):1231-1237.
5. Blois MS (1958). Nature, 29:1199-1200.

P-418: INVESTIGATIONS ON SYNTHESIS AND ANTIOXIDANT ACTIVITY OF SOME PYRAZOLINE DERIVATIVES

[1] Evranos Aksoz, B., [2] Yilmaz Sarialtin, S., [2] Coban, T.

[1]Medicines and Medical Devices Agency, Analyses and Control Laboratories, Ankara, Turkey

[2] Ankara University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

INTRODUCTION:

Antioxidant defensive system in human body protected people from the damages of oxidative stress. Capacity of the defensive system is affected by health status of the individual, diet and age. With the diminishing in capacity of the defensive system, free radicals can cause oxidation of protein, nucleic acids or lipids and toxic products may form. Damages of free radicals produce illnesses such as diabetes, cancer, neural disorders (1). New antioxidants are required to diminish the cumulative effects of oxidative damage. Pyrazoline derivatives have antioxidant activity (2). In this study, we evaluated antioxidant activity of some previously reported pyrazoline derivatives.

MATERIALS AND METHODS:

The free radical scavenging activities of these compounds were tested by the stable radical 2,2, diphenyl-1-picrylhydrazyl (DPPH•) as described by Blois (3). The total antioxidant activity of the samples was measured by [2, 2'-azino-bis(3-ethylbenzthiazoline-6-sulphonic acid)] (ABTS•+) radical cation decolorization assay according to the method of Re et al (4).

RESULTS:

We reported the synthesized pyrazoline derivatives before, for their hMAO inhibitory activities. In this study, all the synthesized compounds were tested for evaluate the antioxidant activity by using in vitro ABTS•+ and DPPH• free radical scavenging activity assays. Except ((3-(5-bromo-2-hydroxyphenyl)-5-(4-methoxyphenyl)-4,5-dihydropyrazol-1-yl)(phenyl) methanone (BEA28), all compounds were found to interact with the stable free radical ABTS•+. However, (3-(5-chloro-2-hydroxyphenyl)-5-(3-methoxyphenyl)-4,5-dihydropyrazol-1-yl)(pyridin-4-yl)methanone (BEA

46) and (3-(2-hydroxy-4-methoxyphenyl)-5-p-tolyl-4,5-dihydropyrazol-1-yl)(pyridin-4-yl)methanone (BEA 61) were found to interact with the stable free radical DPPH• which indicates their radical scavenging activity in an iron-free system where as the others show no effect on it.

CONCLUSIONS:

Compound BEA 46 and BEA 61 were found potent antioxidant compounds for ABTS•+ (IC 50: 0.07 mM and 0.08 mM respectively), and their antioxidant activities are comparable with the known standard, trolox (IC 50: 0.05 mM).

REFERENCES:

1. Kenchappa R, Bodke YD et al., (2017). Arabian Journal of Chemistry, 10 (2):S3895-S3906.
2. Martins DM, Torres BG et al., (2009). Basic & Clinical Pharmacology & Toxicology, 104(2):107-112.
3. Re R, Pellegrini N et al., (1999). Free Radical Biology Medicine, 26(9-10):1231-1237.
4. Blois MS (1958). Nature, 29:1199-1200.

P-419: SYNTHESIS OF NEW BENZOTHIAZOLE-THIADIAZOLE DERIVATIVES AS CHOLINESTERASE AND MONOAMINE OXIDASE INHIBITORS

[1,2] Saglik, BN., [1] Kaya Cavusoglu, B., [1] Kaplancikli, ZA., [1,2] Acar Cevik, U., [1,2] Osmaniye, D., [1,2] Levent, S., [3] Inci, B., [1,2] Ozkay, Y.

[1] Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry,Eskişehir, Turkey

[2] Anadolu University, Faculty of Pharmacy, Doping and Narcotic Compounds Analysis Laboratory, Eskişehir, Turkey

[3] Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Eskişehir, Turkey

INTRODUCTION:

In particular, selective neuronal loss in the brain regions triggers various neurodegenerative diseases such as Alzheimer's disease (AD) and Parkinson's disease (PD). Because of the complex and multifactorial nature of neurodegenerative diseases, it is unlikely that a monotherapy will provide a comprehensive and satisfactory therapeutic solution. Such a therapy is more likely to be obtained by the use of multitarget-oriented ligands, which allow multiple pharmacological properties to be incorporated into a single molecular structure and work synergistically. The strategy of multitarget-directed ligands targeting monoamine oxidases (MAO-A and MAO-B) and cholinesterases (ChE) represents one of the promising approaches due to their neuroprotective, neurorestorative and cognitive enhancing abilities in addition to their effects on monoaminergic neurotransmission (1-3). In this study, we described the synthesis of some new benzothiazole-thiadiazole derivatives as potential anticholinesterase and monoamine oxidase inhibitory compounds.

MATERIALS AND METHODS:

The structure confirmation of the synthesized compounds was performed using FT-IR, 1H-NMR, 13C-NMR, and HRMS spectral data. Th anticholinesterase activity assay of the synthesized compounds was performed using Ellman's spectroscopic method (4). Their inhibitory activity of the compounds against hMAO-A and hMAO-B enzymes was evaluated by using in vitro Amplex Red® reagent based fluorometric method (5). In vitro cytotoxic effects of the final compounds were determined by MTT assay.

RESULTS:

It was observed that the synthesized compounds have promising inhibitory potential against ChE and MAO enzymes. Docking studies of the most active compound 5 revealed that this compound has a notable binding capacity to enzyme active sites.

CONCLUSIONS:

Consequently, synthesized benzothiazole-thiadiazole derivatives have been shown to possess an inhibitory potency of ChE and MAO enzymes.

REFERENCES:

1. Rati KP, Vishnu MS et al., (2017). Journal of Enzyme Inhibition and Medicinal Chemistry,35:37-57.
2. Perrin RJ, Fagan AM et al., (2009). Nature, 461:916-922.
3. Weinstock M (1999). CNS Drugs, 12:307.323.
4. Ellman GL, Courtney KD et al., (1961). Biochemical Pharmacology, 7:88-95.
5. Can NO, Osmaniye D et al., (2018). European Journal of Medicinal Chemistry, 144:68-81.

P-420: NEUROPROTECTIVE EFFECTS OF SOME PYRAZOLINE DERIVATIVES AGAINST 6-OHDA INDUCED NEURODEGENERATION.

[1] Sever, B., [1] Altintop, MD., [1] Ozdemir, A., [2] Kaya Tilki, E., [2] Dikmen, M.

[1] Anadolu University, Department of Pharmaceutical Chemistry, Eskişehir, Turkey

[2] Anadolu University, Department of Pharmacology, Eskişehir, Turkey

INTRODUCTION:

Parkinson's disease (PD) is a common, long-term neurodegenerative disorder characterized by the degeneration of dopaminergic neurons in the substantia nigra pars compacta. Recent studies have reported that oxidative stress plays an important role in the underlying pathology of PD (1). The main aspect of oxidative stress in PD has been investigated with toxin-based models such as 6-hydroxydopamine (6-OHDA) which is based on its ability to generate reactive oxygen species in neurons (2).

MATERIALS AND METHODS:

Owing to the prominence of pyrazolines in the treatment of neurodegenerative disorders (3), herein a series of pyrazoline derivatives (1-9) was synthesized via the treatment of 3-(4-methylphenyl)-1-(furan-2-yl)prop-2-en-1-one (A) with phenylhydrazine hydrochloride derivatives in acetic acid. The neuroprotective effects of these compounds were detected using in vitro 6-OHDA induced neurotoxicity model of PD in PC-12 Adh cell line.

RESULTS:

Treatment with the compounds at 100 µg/mL did not reduce cell viability significantly according to IC50 values and demonstrated their protective effects against cell death in differentiated PC-12 Adh cells treated with 6-OHDA (150 µM) for 24 hours. The reduction in cell viability with 6-OHDA (150 µM) was found 42.91%, whereas the percentages were determined as 28.88, 35.22, 37.24, 30.43, 31.34, 28.97, 19.71, 29.82, and 35.83%, respectively following the treatment with 100 µg/mL of compounds 1-9. According to these results, all compounds might have neuroprotective potential against 6-OHDA induced neurotoxicity in PC-12 Adh cells. In particular, the induction in cell viability% with 1-(4-methylsulfonylphenyl)-3-(2-furyl)-5-(4-methylphenyl)-2-pyrazoline (7) was found to be significant when compared to the 6-OHDA positive control group according to the statistical analysis (**P< 0.01).

CONCLUSIONS:

Compound 7 stands out as a potential neuroprotective agent for further studies in the treatment of PD.

REFERENCES:

1. Youdim et al., (2014). Parkinsonism and Related Disorders, 20S1:S132-136.
2. Drechsel DA, Patel M (2008). Free Radical Biology & Medicine, 44:1873–1886.
3. Alex JM, Kumar R (2017). Journal of Enzyme Inhibition and Medicinal Chemistry, 29: 427-442.

P-421: 1,3,4-THIADIAZOLE DERIVATIVES BEARING BENZYLAMINE MOIETY: SYNTHESIS AND MONOAMINE OXIDASE INHIBITORY ACTIVITY EVALUATION

[1] Kaya Cavusoglu, B., [1] Kaplancikli, ZA., [1,3] Acar Cevik, U., [1,3] Levent, S., [1,3] Osmaniye, D., [1,3] Ozkay, Y., [2] Karaduman, AB., [1,3] Saglik, BN.

[1] Anadolu University, Department of Pharmaceutical Chemistry, Eskişehir, Turkey

[2] Anadolu University, Department of Pharmaceutical Toxicology, Eskişehir, Turkey

[3] Anadolu University, Doping and Narcotic Compounds Analysis Laboratory, Eskişehir, Turkey

INTRODUCTION:

Monoamine oxidase enzymes (MAOs) are flavoenzymes bound to the outer mitochondrial membrane and responsible for the oxidative deamination of neurotransmitters and dietary amines thereby play a vital role in the control of intracellular concentration of them. Since MAO enzymes effect on the metabolism of neurotransmitters, MAO inhibitors have therapeutic interest in search of agents used in the therapy of Alzheimer's, Parkinson's diseases and mental disorders (1,2). There are some studies that confirm 1,3,4-thiadiazole ring and benzylamine moiety possess monoamine oxidase inhibitory potential (3,4). In this study, new 1,3,4-thiadiazole derivates having benzylamine functional moiety were synthesized and their MAO-A and MAO-B inhibitory activities were investigated.

MATERIALS AND METHODS:

The synthesized compounds were tested for their human monoamine oxidase A and B (hMAO-A and hMAO-B) inhibitory potential by an in vitro fluorometric method (5). The chemical structures of the compounds were confirmed by IR, 1H NMR, 13C NMR and MS spectral data.

RESULTS:

Some of the compounds displayed inhibitory activity towards MAO enzymes.

CONCLUSIONS:

In this paper, we detected that the combination of 1,3,4-thiadiazole ring and benzylamine moiety have a contribution on the MAO inhibitory activity.

REFERENCES:

1. Khattab SN, Khalil HH, et al., (2015). Molecules, 20:15976–15988.
2. Riederer P, Lachenmayer L, et al., (2004). Current Medicinal Chemistry, 11:2033–2043.
3. Lucchesini F, Pocci M, et al., (2014). Bioorganic & Medicinal Chemistry, 22:1558–1567.
4. Invidiata FP, Grimaudo S, et al., (1991). Farmaco, 46:1489–1495.
5. Can OD, Osmaniye D, et al., (2017). European Journal of Medicinal Chemistry, 131:92-106.

P-422: ANTINEOPLASTIC EVALUATION OF SEVERAL BENZIMIDAZOLE DERIVATIVES

[1] Kus, C., [2] Yurtcu, E., [2] Korkmaz, Y.

[1] Ankara University, Department of Pharmaceutical Chemistry, Ankara, Turkey

[2]Baskent University, Faculty of Medicine, Department of Medical Biology, Ankara, Turkey

INTRODUCTION:

Benzimidazole nucleus is very important in several categories of therapeutic molecules such as antimicrobial (2,3), proton pump inhibitor (4), antihypertensive (5), anticoagulant, anti-inflammatory, antioxidants (1) have made it an important part in the development of novel therapeutic agents.

MATERIALS AND METHODS:

In this research, benzimidazole nucleus has been used to find novel drugs targeting the human uPA and uPAR systems with potential antineoplastic and antimetastatic activities. Moreover, the cytotoxicity and in vitro anticancer evaluation of the prepared compounds against hepatocellular carcinoma cell and colorectal carcinoma cell lines and the effect of the compounds on the expression of uPA have been assessed.

RESULTS:

5-FU is a reference agent and significantly reduced uPA and uPAR levels in both colorectal and hepatocellular carcinoma cells ($p<0.05$). Compound 2 reduced uPA and uPAR levels in both carcinoma cells ($p<0.05$), too.

CONCLUSIONS:

uPA levels obtained from 2 administration better than 5-FU for both colorectal and hepatocellular carcinoma cells ($p<0.05$). uPAR levels obtaining from 2 administration were similar to 5-FU for both cell lines ($p<0.05$).

REFERENCES:

1. Kus C, Ayhan Kilcigil G, Ozbey S, Kaynak FB, Kaya M, Coban T and Can-Eke B (2008). Bioorganic & Medicinal Chemistry, 16:4294–4303.
2. Tuncbilek M, Tulug K, Altanlar N (2009). Eur J Med Chem, 44:1024–1033.
3. Deepkumar J, and Kalpesh P (2014). Med Chem Res, 23:1290–1299.
4. Iwahi T, Satoh H, Nakao M, Iwasaki T, Yamazaki T, Kubo K, Tamura T, Imada A (1991). Antimicrob Agents Chemother 35:490–496. Shah DI, Sharma M, Bansal Y, Bansal G, Singh M (2008). Eur J Med Chem, 43:1808–1812.

P-423: SYNTHESIS AND BIOLOGICAL ACTIVITIES OF 4-(5-CHLORO-6-FLUORO-1H-BENZO[D]IMIDAZOL-2-YL)-N-ISOPROPYLBENZAMIDINE.HCL

[1] Kus, C., 2 Altanlar, N., [3] Basaran, R., [3] Can Eke, B.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Ankara, Turkey

[3]Ankara University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

INTRODUCTION:

Benzamidine group is an attractive target for complexation studies. It has a very important place in the drug class (1). In this study, we prepared 4-(5-chloro-6-fluoro-1H-benzo[d]imidazol-2-yl)-N-isopropyl benzamidine.HCl. Biological activity studies of it were displayed.

MATERIALS AND METHODS:

Herein, synthesis, antimicrobial and antioxidant activity evaluation of 4-(5-chloro-6-fluoro-1H-benzo[d] imidazol-2-yl)-N-isopropyl benzamidine.HCl (7) were reported. Condensation of the 3-chloro-4-fluoro-o-phenylenediamine with the Na2S2O5 adduct of 4-cyanobenzaldehyde gave compound 5. The nitrile group of compound 5 was converted to iminester 6. The final compound 7 was obtained via reaction of iminester with isopropanol.

RESULTS:

The assigned structure was substantiated by IR, 1H NMR, and MS analysis data. All data were seen as expected. Antioxidant properties of compound 7 was evaluated by determination of microsomal NADPH-dependent inhibition of lipid peroxidation levels (LP assay) and microsomal ethoxyresorufin O-deethylase activity (EROD assay) was investigated. At the same time, the antimicrobial activity of compound 7 was evaluated.

CONCLUSIONS:

Compound 7 showed activity as 25 µg/ml against Staphylococcus aureus and it has 82 % EROD activity. Compound 7 has a similar EROD activity as caffeine.

REFERENCES:

1. Bell TW and Santora VJ (1992). American Chemical Society, 114, 8300-8302.

P-424: INVESTIGATION OF ANTIMICROBIAL PROPERTIES OF SOME BENZOXAZOLE DERIVATIVES

[1] Acar, C., [1] Temiz Arpaci, O., [2] Kaynak Onurdag, F., [2] Okten, S.

[1] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

[2] Trakya University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Edirne, Turkey

INTRODUCTION:

Microbial infectious diseases continue to be the one of the leading causes of morbidity and mortality. Antibiotics and antimicrobial agents are still the most potent weapons to fight against bacterial infections, but the evolution of resistance has increasingly been becoming problem. Benzoxazoles constitute an important class of heterocyclic compounds with antimicrobial activity (1-3).

MATERIALS AND METHODS:

The benzoxazoles [2 – 8] were evaluated for their antimicrobial activity with microdilution technique described by CLSI (4-5), against some Gram-positive/ negative bacteria and fungus Candida albicans and their drug-resistant isolates in comparison with standard drugs.

Results and Discussion: The minimum inhibitory concentrations (MIC) of the new some benzoxazoles, were determined against standard bacterial and fungal strains and drug-resistant isolates and compared to those of several reference drugs and all the observed in vitro antimicrobial activity results of the tested compounds are given Table 1.

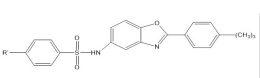


Table 1. Antimicrobial activity results (MIC µg/ml) of synthesized compounds **2-8** with the standard drugs.

	R	A	B	C	D	E	F	G	H	I
2	H	128	128	128	128	128	128	128	64	>512
3	F	128	128	128	128	128	128	128	64	>512
4	Cl	128	128	128	128	128	128	128	64	>512
5	Br	128	128	128	128	128	128	128	64	>512
6	CH_3	128	128	128	128	128	128	128	64	>512
7	OCH_3	128	128	128	128	128	128	128	64	>512
8	NO_2	128	128	128	128	128	128	128	64	>512
Vancomycin		-	-	-	-	<0.0625	<0.0625	<0.0625	<0 (R)	-
Ampicillin		2	2	-	-	2	>8 (R)	2	>8 (R)	-
Meropenem		<0.0625	<0.0625	0.5	0.5	<0.0625	>8 (R)	2	-	-
Ciprofloxacin		<0.0625	<0.0625	1	2 (R)	0.5	0.5	2	2	-
Gentamicin		0.25	0.25	0.5	>8 (R)	1	2 (R)	-	-	-
Amphotericin B		-	-	-	-	-	-	-	-	0.5

A: *E. coli* ATCC 25922, B: *E. coli* isolate, C: *Pseudomonas aeruginosa* ATCC 27853, D: *P. aeruginosa* isolate, E: *Staphylococcus aureus* ATCC 29213, F: MRSA, G: *Enterococcus faecalis* ATCC 29212, H: VRE, I: *Candida albicans* ATCC 10231 (R): Resistant (according to CLSI and EUCAST)

CONCLUSIONS:

In this study, we aimed to develop new effective antimicrobial agents possessing benzoxazole nuclei in their structure. So, we put a para-substituted-phenyl sulfonylamido moiety on fifth position and a lipophilic group that is a para-tert-butylphenyl moiety on second position of benzoxazole ring. Microbiological results showed that new benzoxazole derivatives possess an antimicrobial activity having MIC values of 64-128 µg/ml against the tested microorganisms except for C. albicans and the standard drugs were more active against the tested pathogens.

REFERENCES

1. Prudhomme M, Guyot J, Jeminet G (1986) J. Antibiot. 39:934-937.
2. Yildiz-Oren I, Tekiner B, Yalcin I, Temiz Arpaci O, Aki Sener E, Altanlar N (2004) Archiv der Pharmazie, 337(7):402-410
3. Akı Sener E, Temiz Arpaci O, Yalcin I, Altanlar N. (2000), II Farmaco, 55: 397-405
4. Clinical and Laboratory Laboratory Standards Institute (CLSI) (formerly NCCLS): Performance Standards for Antimicrobial Susceptibility Testing; 16th Informational Supplement. CLSI M100-S18. Clinical and Laboratory Standards Institute, 940 West Valley Road, Wayne, Pennsylvania, USA, 2008.
5. Clinical and Laboratory Standards Institute (CLSI) (formerly NCCLS): Reference method for broth dilution antifungal susceptibility testing yeast, approved standard, M27-A3. Clinical and LaboratoryStandards Institut

P-425: SYNTHESIS OF SOME 6,7-DIMETHOXY QUINAZOLINE DERIVATIVES AS EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) TYROSINE KINASE INHIBITORS

Acar, C., Altuntas, TG., Goker, H.

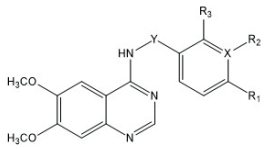
Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

INTRODUCTION:

Cancer is one of the most widespread and feared diseases in the world today, because it is known to be difficult to cure (1). The aberrant activity of EGFR has been involved in the pathogenesis and progression of different types of tumors (2, 3). Accordingly, it has been regarded as an attractive target for cancer therapy and many anti-EGFR inhibitors including small molecule Tyrosine Kinase Inhibitors (TKIs) have been developed and investigated (3). 4-Anilinoquinazoline-based derivatives represent an attractive scaffold for small molecular EGFR-TKIs in the field of medicinal chemistry (4).

MATERIALS AND METHODS:

In the present study, new series of quinazolines have been synthesized and will be screened in vitro for antitumor activity. First, Methyl 2-amino-4,5-dimethoxybenzoate was reacted with formamide to give 6,7-dimethoxyquinazolin-4-ol. Treatment of the quinazolinol with thionyl chloride formed 4-chloro-6,7-dimethoxyquinazoline. Chloride atom was then reacted with various amines to afford the desired quinazolines.



	R_1	R_2	R_3	X	Y
1	F	CF_3	H	C	-
2	Cl	Cl	Cl	C	-
3	H	H	Cl	N	-
4	CN	H	H	C	-
5	CN	H	Cl	C	-
6	H	CN	H	C	-
7	CN	H	H	C	CH_2

RESULTS:

Compounds 2, 3, 5, 7 (Figure) were prepared for the first time. The 1H-NMR, 13C-NMR and mass spectra results of all compounds agree with those of the proposed structures.

CONCLUSIONS:

In the present investigation, we aimed to develop new effective anticancer agents possessing quinazoline analogues. Consequently, a series of new N-(substituted phenyl)-4-amino-6,7-dimethoxyquinazolines and N-(substituted pyridine-3-yl)-4-amino-6,7-dimethoxyquinazoline were synthesized and the structures of the new derivatives were elucidated by spectral techniques.

REFERENCES:

1. Mubeen M, Kini SG (2012). International Journal of Therapeutic Applications. 5:29-37.
2. Yarden Y (2001). European Journal of Cancer. 37:3-8.
3. Lee DH (2017). Pharmacology & Therapeutics. 174:1-21.
4. Chang J, Ren H, Zhao M, Chong Y, Zhao W, He Y et al. (2017). European Journal of Medicinal Chemistry. 138:669-688.

P-426: EVALUATION OF MELATONIN AND NEW SYNTHETIC ANALOGUES AS ANTIOXIDANT AND CYP1 INHIBITOR.

[1] Karaaslan, C., [1] aNeuhaus, E., [2] Ince, E., [2] Tascioglu, A., [3] Shirinzadeh, H., [2] Gurer Orhan, H., [1] Suzen, S.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey. (a:Exchange student of Leonardo DaVinci Programme from Martin Luter University Halle Wittenberg Institution of Pharmacy, Halle Germany)

[2]Ege University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Izmir, Turkey

[3]Erzincan University, Faculty of Pharmacy Department of Pharmaceutical Chemistry, Erzincan, Turkey

INTRODUCTION:

Over the last decade, there has been substantial growth in the field of melatonin (MLT) and use of MLT-like compounds in the treatment of several diseases. MLT is *is* a hormone that *is* produced by the pineal gland in animals. It is also detected in non-vertebrates like bacteria and fungus as well as endogenously produced in edible plants. MLT can scavenge different reactive oxygen species and can also stimulate the synthesis of antioxidant enzymes.

MATERIALS AND METHODS:

Our ongoing study relies on changing the groups in the different modifiable sites of the indole ring to increase the antioxidant activity. In this study a new approach for substitution of indole ring as indole-based MLT analogue was proposed. We report the synthesis and characterization of a series of new indole-7-aldehyde hydrazide/hydrazone derivatives as indole-based MLT analogues. Anticancer potential of the compounds were evaluated both by their antioxidant and CYP1 inhibitory activities. Antioxidant capacity of the compounds was investigated in a cell-based (DCFH assay) and a cell-free (DPPH assay) in vitro assays. Potential inhibitory effects of the compounds on CYP1 catalytic activity were investigated via EROD assay. Cytotoxic activity of the compounds was further evaluated by the MTT assay in CHO-K1 cells.

RESULTS:

MLT analogues having an o-halogenated aromatic moiety exhibited effective antioxidant properties without having any cytotoxic effect.

CONCLUSIONS:

MLT derivatives represent promising scaffolds for discovery of effective antioxidant agents.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (109S099)

P-427: ANTIOXIDANT PROPERTIES OF CARBAZOLE DERIVATIVES; EVALUATION OF THE ACTIVITY ON AMYLOID B-INDUCED DAMAGE

[1] Karaaslan, C., [2] Ince, E.,[3] Tavakkoli, M.,[3] Firuzi, O.,[4] Saso, L., [2] Gurer Orhan, H., [1] Suzen, S.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey,

[2]Ege University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Izmir, Turkey,

[3]Medicinal and Natural Products Chemistry Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

4Sapienza University of Rome, Department of Physiology and Pharmacology "Vittorio Erspamer", P. le Aldo Moro 5, 00185 Rome, Italy

INTRODUCTION:

Antioxidants could be helpful for prevention of several diseases related with oxidative stress including neurodegenerative disorders. Carbazoles have been reported to exhibit diverse biological activities such as antimicrobial, antitumor, antiepileptic, antihistaminic, antioxidative, anti-inflammatory, antidiarrhoeal,

analgesic, neuroprotective and pancreatic lipase inhibition properties. Recently, it has been shown to exhibit promising antioxidant activities.

MATERIALS AND METHODS:

A series of 9-ethyl-9H-carbazole hydrazone derivatives were synthesized, purified and chemical structures are characterized using NMR (1H,13C), Mass Spectrometer and Elemental Analysis. Their in vitro antioxidant activity and possible cytotoxic effects were investigated.

RESULTS:

Newly synthesized carbazoles were found to have radical scavenging activity with a varying potency both in cell-free and cell-based in vitro assays. Several compounds were found to have cytotoxic activity, however this cytotoxic activity was not more than melatonin. Several compounds also significantly protected neuronal PC12 cells against amyloid β-induced damage, which reflects their capacity as neuroprotective agents.

CONCLUSIONS:

These findings might provide an alternative strategy for development of novel carbazole derivatives for management of neurodegenerative diseases such as Alzheimer's disease. This work was supported by the Scientific and Technological

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (109S099) and Shiraz University of Medical Sciences (grant number: 94-01-12-10056)

P-428: SYNTHESIS AND STRUCTURAL CHARACTERIZATION OF SOME THIOSEMICARBAZIDES DERIVED FROM INDOMETHACIN

[1,2] Yilmaz, D, [1] Yanik, H, [1] Yilmaz, O, [2] Kucukguzel, SG.

[1]TUBITAK Marmara Research Center, Kocaeli, Turkey

[2] Marmara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Istanbul, Turkey

INTRODUCTION:

Due to the importance of indole ring and thiosemicarbazide moiety in medicinal chemistry area (1-4), novel indol based thiosemicarbazide compounds were synthesized by using indomethacin as a starting material.

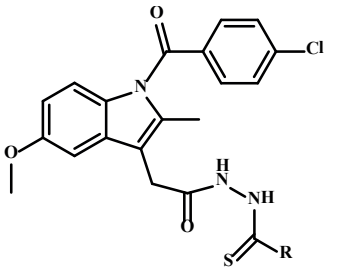
MATERIALS AND METHODS:

Indomethacin, [1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]acetic acid, converted their ester (1) which is followed by reacted with hydrazine hydrate to form hydrazide derivative (2). Reaction of compound 2 and several isothiocyanates yielded N-alkyl/aryl thiosemicarbazides (3).

RESULTS:

The aim of this study is to synthesize novel indol based thiosemicarbazide derivatives and confirm their structures by FT-IR, 1H-NMR and elemental analysis data.

Conclusion: Indol based thiosemicarbazide derivatives were synthesized and their structures were confirmed by FT-IR, 1H-NMR and elemental analysis data.



R= Alkyl/Aryl Groups

Figure: Indol based thiosemicarbazide compounds [3]

REFERENCES:

1. Yılmaz O, Turan SO, Akbuğa J, Tiber PM, Orun O, Supuran CT, Kucukguzel SG (2015). Journal of Enzyme Inhibition and Medicinal Chemistry, 30(6): 967-980.
2. Çıkla P, Arora P, Basu A, Talele TT, Kaushik-Basu N, Kucukguzel SG (2013). Marmara Pharmaceutical Journal, 17, 138-146.
3. Kucukguzel SG, Coskun GP (2016). Anti-Cancer Agents in Medicinal Chemistry, 16(10): 1288-1300.
4. Dadas Y, Coskun GP, Bingol ÖA, Özsavci D, Kucukguzel SG (2015). *Marmara Pharmaceutical* Journal, 19: 259-267.

P-429: SYNTHESIS OF NEW THIAZOLYLHYDRAZINE DERIVATIVES AS MONOAMINOXIDASE INHIBITORS

[1,2] Osmaniye, D., [1,2] Levent, S., [1,2] Ozkay, Y., [1] Kaplancikli, ZA., [1,2] Saglik, BN., [1] Cavusoglu Kaya, B., [3] Inci, B., [1,2] Acar Cevik, U.

[1]Anadolu University, Faculty of Pharmacy Eskişehir, Department of Pharmaceutical Chemistry Eskişehir, Turkey

[2]Anadolu University, Faculty of Pharmacy, Doping and Narcotic Compounds Analysis Laboratory, Eskişehir, Turkey

[3]Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Eskişehir, Turkey

INTRODUCTION:

MAO (Monoamine oxidase) a flavoprotein located at the outer membrane of mitochondriain neuronal, glial, and other cells are extensive enzymes that play a key role in the degradation of exogenous and endogenous amines. MAO including two isoforms, namely MAO-A and MAO-B can be separated by their individual substrate preferences. MAO-A oxidizes norepinephrine and serotonin [5-hydroxytryptamine, 5-HT], while MAO-B preferentially deaminates 2-phenylethylamine (2-PEA) and benzylamine. Actually, hMAO-B is responsible for >80% of the MAO activity in the brain, where it metabolizes dopamine and other amines in serotonergic and histaminergic neurons and astrocytes. In addition hMAO-B activity is considerably higher in the brains of patients with Alzheimer's and Parkinson's disease (PD) (1-3) During the last five decades, there are a number of studies in the literature corresponding with thiazolylhydrazine derivatives display hMAO inhibitory activity in the range of micromolar concentration (3,4). Prompted from above information, in this study we designed and synthesized new thiazolylhydrazine derivatives as potential MAO inhibitors.

MATERIALS AND METHODS:

The structures of the synthesized compounds were elucidated using FT-IR, 1H-NMR, 13C-NMR, and HRMS spectral data. The inhibitory activity of the obtained compounds against hMAO-A and hMAO-B enzymes was evaluated by using in vitro Amlex Red® reagent based fluorometric method (5).

RESULTS:

It was observed that the synthesized compounds displayed inhibitory activity against both MAO isoforms to different extends.

CONCLUSIONS:

Consequently, synthesized thiazolylhydrazine derivatives have been shown to possess an inhibitory potency of MAO enzymes.

REFERENCES:

1. Chimenti F, Carradori S et al., (2010). Eur. J. Med. Chem, 45:800-804.
2. Distinto S, Meleddu R et al., (2016). Eur. J. Med. Chem, 108:542-552.
3. Chimenti P, Petzer A et al., (2013). Eur. J. Med. Chem, 66:221-227.
4. Can NO, Osmaniye D et al., (2018). Eur. J. Med. Chem, 144:68-81.
5. Can OD, Osmaniye D et al., (2017). Eur. J. Med. Chem, 131:92-106.

P-430: SYNTHESIS AND CHARACTERIZATION OF NOVEL INDOLE DERIVATIVES

Cosar, ED., Demiray S., Ulusoy Guzeldemirci N.

Istanbul University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Istanbul, Turkey

INTRODUCTION:

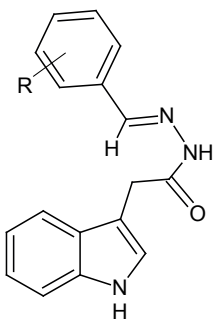
Indole and its derivatives display an extensive range of biological activities such as anticancer (1), analgesic and anti-inflammatory (2) and carbonic anhydrase inhibition activities (3). In view of the literature data reported above we synthesized a series of new indole derivatives.

MATERIALS AND METHODS:

Melting points were determined on a Büchi B-540 melting point apparatus in open capillary tubes and are uncorrected. Elemental analyses were done on a Thermo Finnigan Flash EA 1112 elemental analyzer. IR spectra were recorded on KBr discs, using a Shimadzu IR Affinity-1 FT-IR spectrophotometer. 1H-NMR spectra were measured on a Varian UNITY INOVA (500 MHz) spectrometer using DMSO-d6.

RESULTS:

Hydrazide and suitable aryl aldehyde were heated in ethanol to yield N'-(substituted benzylidene)-2-(1H-indole-3-yl)acetohydrazide derivatives (Scheme 1). Structures of title compounds were confirmed based on their spectral and analytical data.



Scheme 1. Synthesized compounds

CONCLUSIONS:

A series of new hydrazide-hydrazones bearing indole moieties were synthesized. The new compounds were characterized by spectral data (IR, 1H-NMR) and elemental analyses. Structures proposed have been confirmed by spectral data.

ACKNOWLEDGEMENTS:

This work was supported by Istanbul University Scientific Research Projects. Project Number: 40810.

REFERENCES:

1. Oliveira JF, Lima TS, Vendramini-Costa DB, Batistade Lacerda Pedrosa SC, Lafayette EA, Ferreirada Silva RM, Vitalinode Almeida SM, Olímpiode Moura R, Ruiz ALTG, Ernestode Carvalho J, Alves de Lima MC (2017). Eur J Med Chem, 136:305-314.
2. Anekal DP, Biradar JS (2017). Arabian J Chem, 10:S2098-S2105.
3. Eldehna WM, Al-Ansary GH, Bua S, Nocentini A, Gratteri P, Altoukhy A, Ghabbour H, .Ahmed HY, Supuran CT (2017). Eur J Med Chem, 127:521-530.

P-431: IN VITRO AND IN SILICO STUDIES OF A SERIES OF 1,3,4-THIADIAZOLES AS ACETYLCHOLINESTERASE INHIBITORS

[1] Altintop, MD., [1] Sever, B., [1] Ozdemir, A., [1] Zeytun, E., [2] Temel, HE.

[1] Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskişehir, Turkey

[2] Anadolu University, Faculty of Pharmacy, Department of Biochemistry, Eskişehir, Turkey

INTRODUCTION:

Alzheimer's disease (AD) is the most common form of dementia, affecting 4-8% of the elderly population across the globe (1). Despite extensive efforts devoted to the discovery of potent anti-AD drugs, three cholinesterase inhibitors (donepezil, galantamine, rivastigmine) and memantine (N-methyl-D-aspartate receptor antagonist) are the only drugs currently used for the management of AD (1,2). These agents only provide symptomatic relief but do not halt the progression of the disease (2). Due to the urgent need to develop new anti-AD drugs (1,2), herein we aimed to evaluate the inhibitory effects of a series of 1,3,4-thiadiazoles on acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE).

MATERIALS AND METHODS:

N-(Alkyl/aryl)-2-[(5-((4-nitrophenyl)amino)-1,3,4-thiadiazol-2-yl)thio]acetamide derivatives (1-8) were evaluated for their inhibitory effects on AChE and BuChE using a modification of Ellman's spectrophotometric method. Molecular docking studies were also carried out for the most effective compounds in the active site of AChE (3). The X-ray crystallographic structure of AChE complex with donepezil was retrieved from the Protein Data Bank server (PDB code: 4EY7).

RESULTS:

N,N-diethyl-2-[(5-((4-nitrophenyl)amino)-1,3,4-thiadiazol-2-yl)thio]acetamide (1) and N-(1,3-benzodioxol-5-ylmethyl)-2-[(5-((4-nitrophenyl)amino)-1,3,4-thiadiazol-2-yl)thio] cetamide (5) were identified as the most potent AChE inhibitors in this series with IC50 values of 9.87±0.32 μg/mL and 11.73±0.31 μg/mL, respectively. Compounds 1 and 5 showed good affinity to the active site of AChE forming π-π interactions with Trp286 residue due to their 4-nitrophenyl moieties. The benzodioxole ring system of compound 5 also presented π-π interactions with Trp86 residue. On the other hand, the tested compounds did not show any significant BuChE inhibitory activity.

CONCLUSIONS:

According to the in vitro and in silico studies, compounds 1 and 5 stand out as promising candidates for further studies.

REFERENCES:

1. Godyń J, Jończyk J, Panek D, Malawska B (2016). Pharmacological Reports, 68:127-138.
2. Tayeb HO, Yang HD, Price BH, Tarazi FI (2012). Pharmacology & Therapeutics, 134:8-25.
3. Schrödinger Release 2016-2: Schrödinger, LLC, New York, NY, USA.

P-432: STUDIES ON THE SYNTHESIS OF SOME NEW FLAVONE SULFONAMIDE COMPOUNDS AS ANTICANCER AGENTS AND HDAC6 INHIBITORS

Sari, E., Bozdag Dundar, O.

Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

INTRODUCTION:

Histone deacetylases (HDAC) can affect many vital regulatory processes, including gene expression, mRNA stability, protein interactions, protein stability, and enzymatic activity via the removal of acetyl groups attached to lysine residues in histone and non-histone proteins. HDAC6 which is the one of the non-histone deacetylase has become a target for treatment of serious diseases like cancer, Alzheimer and autoimmune disorders 1,2). HDAC6 is responsible for deacetylation of non-histone cytoplasmic proteins such as microtubule (α/β tubulin), Hsp90 (heat shock protein 90), cortactin and chaperon. Inhibition of HDAC6 results in the loss of microtubule stability and

function and causes increased protein aggregation (3). Using these disadvantages as an advantage in favor of cancer treatment, histone deacetylase 6 inhibitors (HDAC6i) are valuable pharmacological targets.

MATERIALS AND METHODS:

A mixture of 5-methoxyflavonesulfonylpiperazine, appropriate acyl chloride/bromide compounds, Na2CO3 and 10 ml dimethylformamide were stirred at room temperature for 48 h.

RESULTS:

In this study, in the light of anticancer properties of HDAC6i, flavon sulfonamide compounds have been synthesized. The structural evaluation of the synthesized compounds was based on the 1H NMR, Mass and elementary analysis data. Their cytotoxic activity are under investigation. We are expecting that synthesized compounds can bind the enzymes active site and make the inhibition of HDAC6.

CONCLUSIONS:

Their docking studies are shown that they have enough interactions for the HDAC6 enzyme inhibition. Synthesized new flavone compounds are under investigation within the scope of anticancer properties and HDAC6 inhibitory activities.

ACKNOWLEDGEMENTS:

This work was supported by Research Organization of Ankara University, Turkey (No:17L0237003).

REFERENCES:

1. Li Y, Shin D, Kwon SH. FEBS J. 2013;280:775.
2. Lin X, Chen W, Qiu Z, Guo L, Zhu W, Li W, Wang Z, Zhang W, Zhang Z, Rong Y, Zhang M, Yu L, Zhong S, Zhao R, Wu X, Wong JC, Tang G. Journal of Medicinal Chemistry.2015;58:2809-20.
3. Namdar M, Perez G, Ngo L, Marks PA, PNAS. 2010;107:20003-20008.

P-433: SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF NEW ARYL SULFONYL HYDRAZONES

[1] Karakucuk Iyidogan, A., [1] Oruc Emre, EE., [1] Koseli, MB., [2] Aygun, A., [2] Sen, F.

[1]Gaziantep University, Faculty of Arts and Sciences, Department of Chemistry, Gaziantep, Turkey

[2] Dumlupınar University, Faculty of Arts and Science, Department of Biochemistry, Sen Research Group,Kutahya, Turkey

INTRODUCTION:

Sulfonyl hydrazone scaffold has important role in medicinal chemistry and exhibited different biological activities such as antioxidant, anticancer, anticonvulsant, antidepressant, antimicrobial, anticholinesterase,analgesic and anti-inflammatory activities (1,2).

MATERIALS AND METHODS:

4-fluorobenzenesulfonyl hydrazones were obtained by the reaction of 4-fluorobenzenesulfonyl hydrazide with some substituted aldehydes in methanol. Physical and chemical properties of compounds have been characterized and comfirmed by IR, 1H-NMR, 13C-NMR, mass spectroscopy and elemental analysis. For the bacterial culture; first, Nutrient Broth liquid culture was prepared to replicate the bacteria (Staphylococcus aureus, Enterococcus-faecalis, E-coli, Klebsiella-pneumoniae). These bacterias were added to the liquid media and kept at 37 oC for a day in a shaking incubator. After 24 hours, drug concentrations were tested at different concentrations on bacterial cultures. The MIC (minimum inhibition concentration) value was obtained after the culture study. MBC (minimum bactericidal concentration) value was found by using MIC value (3,4).

RESULTS:

All compounds have been performed for antimicrobial performance against several bacterias such as Staphylococcus aureus, Enterococcus-faecalis, E-coli, Klebsiella-pneumoniae) bacteria. Minimum inhibitor and bactericidal concentration (MIC and MBC) values were examined in these experiments. It was observed that the 4-fluorobenzenesulfonyl hydrazones has potential antimicrobial effect in accordance with the outcome results.

CONCLUSIONS:

As a conclusion, the antimicrobial activity of sulfonyl hydrazones was reported. The prepared sulfonyl hydrazones compounds indicated very good antimicrobial performance for mentioned bacterial cultures.

REFERENCES:

1. Karaman N, Oruç Emre EE, et al., (2016). Medicinal Chemistry Research, 25:1590-1607.
2. Kendall JD, Giddens AC, et al., (2017). Bioorganic and Medicinal Chemistry Letters, 27:187-190.
3. Tânia CSP, Pires MID, et al., (2018). Food Chemistry, 240:701-706.
4. Jayanta KP, Gitishree D, et al., (2016). Journal of Photochemistry and Photobiology, B: Biology, 161:200–210.

P-434: SYNTHESIS AND CHARACTERIZATION OF NOVEL AMIDE DERIVATIVES BEARING MORPHOLINE RING

Oruc Emre, EE., Ece, S., Karakucuk Iyidogan, A.

Gaziantep University, Faculty of Arts and Sciences, Department of Chemistry, Gaziantep, Turkey.

INTRODUCTION:

Amide derivatives have been demonstrated to posses anticonvulsant, antimicrobial, analgesic, antiinflammatory and anticancer activities. In this research, a series of amide derivatives bearing morpholine ring were synthesized (1,2).

MATERIALS AND METHODS:

2-Chloro-N-[4-(morpholin-4-yl)phenyl]acetamide was obtained by the reaction of 4-morpholinoaniline with chloroacetyl chloride in dioxane. The acetamide derivative was reacted with various amines to obtain N-[4-(morpholin-4-yl)phenyl]-2-substituted acetamides (3). The structures of these amide derivatives were confirmed by IR, 1H NMR, 13C NMR and mass spectral data besides elemental analysis.

RESULTS:

In the ^{1}H NMR spectra, the amide -NH- signals appeared as a singlet at 9.53-10.07 ppm. The CH2 resonances of amide compounds were observed at 3.08-4.20 ppm. All the aromatic protons were observed at the expected region in their NMR spectrum.

CONCLUSIONS:

All spectral data were consistent with the proposed structures. The new amide compounds will be tested for their antioxidant and anticholinesterase activities.

REFERENCES:

1. Harte AJ, Gunnlougsson T (2006). Tetrahedron Letters, 47:6321-6324.
2. Patel RV, Patel PK et al., (2012). European Journal of Medicinal Chemistry, 53:41-51.
3. Koçyigit Kaymakcioglu B, Toklu HZ et al. Journal of Enzyme Inhibition and Medicinal Chemistry, 23:454-461.

P-435: SYNTHESIS AND EVALUATION OF NEW PYRAZOLINE DERIVATIVES AS ANTIBACTERIAL AGENTS.

[1] Ozdemir, A., [1] Altintop, MD., [1] Sever, B., [2] Bulbul, EF., [3] Karadag, AE.

[1] Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskişehir, Turkey

[2] Istanbul Medipol University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Istanbul, Turkey

[3] Istanbul Medipol University, Faculty of Pharmacy, Department of Pharmacognosy, Istanbul, Turkey

INTRODUCTION:

Pyrazoline has been recognized as a structural core for building a huge variety of biologically active agents. The therapeutic applications of pyrazolines extend from central nervous system applications to antimicrobials (1). In particular, the significance of pyrazolines as antimicrobial agents prompted us to design and synthesize pyrazoline-based antibacterial agents.

MATERIALS AND METHODS:

New thiazolyl-pyrazoline derivatives (Fig. 1) were synthesized and evaluated for their antibacterial effects on S. aureus, E. coli, E. faecalis, B. subtilis, S. typhi and P. aeruginosa using a broth microdilution assay. Amoxicillin, tetracycline, clarithromycin were used as standard drugs.

RESULTS:

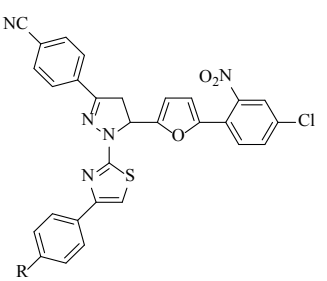
The synthesized compounds were found to be effective on B. subtilis and E. faecalis. According to MIC values, compounds 2, 4, 6 and 8 were more effective on B. subtilis than all standard drugs. In particular, methylsulfonyl-substituted compound 8 was identified as the most potent antibacterial agent with a MIC value of 3.9 μg/μL in this series.

CONCLUSIONS:

Further studies are needed to clarify the mechanism of action for the antibacterial activity of compound 8.

REFERENCES:

1. Shaaban MR, Mayhoub AS, Farag AM (2012). Expert Opinion on Therapeutic Patents, 22(3):253-291.



Compound	R
1	H
2	Cl
3	Br
4	OCH_3
5	F
6	NO_2
7	CN
8	SO_2CH_3

Figure 1. The structures of compounds 1-8

P-436: NEW THIAZOLYL-PYRAZOLINE DERIVATIVES AS ANTIBACTERIAL AGENTS.

[1] Ozdemir, A., [1] Altintop, MD., [1] Sever, B., [2] Bulbul, EF., [3] Karadag, AE.

[1] Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskişehir, Turkey

[2] Istanbul Medipol University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Istanbul, Turkey

[3] Istanbul Medipol University, Faculty of Pharmacy, Department of Pharmacognosy, Istanbul, Turkey

INTRODUCTION:

Thiazoles and pyrazolines have attracted a great deal of interest due to their pivotal role in medicinal chemistry as therapeutic agents ranging from antibacterial agents to diuretics (1,2). As a result, herein we aimed to design and synthesize antibacterial agents based on molecular hybridization of thiazole and pyrazoline scaffolds.

MATERIALS AND METHODS:

New thiazolyl-pyrazoline derivatives (1-8) (Fig. 1) were synthesized and evaluated for their antibacterial effects on S. aureus, E. coli, E. faecalis, B. subtilis, S. typhi and P. aeruginosa using a broth microdilution assay. Amoxicillin, tetracycline, clarithromycin were used as standard drugs.

RESULTS:

It was observed that the synthesized compounds were effective on E. faecalis. Compounds 2, 5, 6 and 8 were identified as the most effective compounds in this series on E. faecalis with a MIC value of 15.6 µg/mL. Compound 6 (MIC= 31.2 µg/mL) was also found to be more effective on S. aureus than other compounds. Additionally, compound 2 was the most effective compound in this series on E. coli with a MIC value of 31.2 µg/mL.

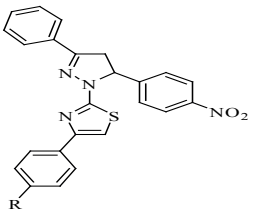
CONCLUSIONS:

In the view of this work, further studies are needed to clarify the mechanism of action for the antibacterial activities of compounds 2, 5, 6 and 8.

REFERENCES:

1. Chhabria MT, Patel S, Modi P, Brahmkshatriya PS (2016). Current Topics in Medicinal Chemistry, 16:2841-2862.

2. Shaaban MR, Mayhoub AS, Farag AM (2012). Expert Opinion on Therapeutic Patents, 22(3):253-291.



Compound	R
1	H
2	Cl
3	Br
4	OCH_3
5	F
6	NO_2
7	CN
8	SO_2CH_3

Figure 1. The structures of compounds 1-8

P-437: SYNTHESIS OF SOME NEW BENZOXAZOLES AS HTOPO IIA INHIBITORS

[1] Karatas, E., [2] Foto, E., [3] Zilifdar, F., [1] Yildiz I.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

[2]Necmettin Erbakan University, Faculty of Science, Department of Biotechnology, Konya, Turkey.

[3]Hacettepe University Faculty of Science, Department of Molecular Biology, Ankara, Turkey

INTRODUCTION:

DNA topoisomerases are nuclear enzymes that make transient strand breaks in DNA to allow a cell to manipulate its topology (1,2). DNA topoisomerases have been classi- fied into two types. Type I DNA topoisomerase breaks and rejoins only one of the two strands during catalysis, while type II DNA topoisomerase acts on both strands for each DNA strand-passing reaction and it requires ATP for full activity (3). Investigation of inhibitory activities of eukaryotic topoisomerases is widely used in anticancer drug development. The aim of this study is that exploring a new benzoxazole derivatives as anticancer compounds targeting hTopo IIα.

MATERIALS AND METHODS:

The derivatives were synthesized by heating 2-amino-4-nitrophenol with suitable acid in 24 g polyphosphoric acid (PPA) and stirring for 2-3 hours at 120 -130°C. Human DNA Topoisomerase IIα inhibition activity of benzoxazoles was performed by using DNA relaxation assay in a cell free system.

RESULTS:

In this study, we have synthesized some 2-substitutedphenyl-5-nitrobenzoxazole derivatives and investigated their hTopo IIα enzyme inhibition effects. All tested compounds showed moderate inhibition activity for h Topo IIα enzyme. Moreover, their activity were compared to clinically used Topo II inhibitor drug, etoposide.

CONCLUSIONS:

Some 5-nitrobenzoxazoles as possible hTopo IIα enzyme inhibitors were synthesized in order to develope new antitumor compounds. According to this work, it can be considered that the para position of the phenyl moiety in the second position of the benzoxazole is very important for advanced anticancer investigations.

REFERENCES:

1. Champous JJ (2001). Annu Rev Biochem, 70:369–413.
2. Wang JC (2002). Nat Rev Mol Cell Biol, 3:430–440.
3. Nitiss JL (1998). Biochim Biophys Acta, 1400:63–81.

P-439: DESIGN, SYNTHESIS AND BIOLOGICAL EVALUATION OF NICOTINATE DERIVATIVES FOR CANCER THERAPY

[1] Tok, F., [1] Kocyigit Kaymakcioglu, B., [2] Gunal, S., [2] Ilhan, R., [2] Ballar Kirmizibayrak, P.

[1] Marmara University, Department of Pharmaceutical Chemistry, Istanbul, Turkey

[2] Ege University, Department of Biochemistry, Izmir, Turkey

INTRODUCTION:

Urea and carbohydrazide are important functional groups exhibiting a variety of biological activities. PARP-1 enzyme, repairs DNA damage, is a new target for cancer therapy. In this study, a series of new urea and carbohydrazide derivatives containing an pyridine ring were designed and synthesized (1, 2).

MATERIALS AND METHODS:

In the first step, nicotinate derivatives bearing amine group were solved in acetone and urea compounds were synthesized with substituted isocyanates. In the second step, ester functional group was converted to the hydrazide group in ethanol with reflux. In the last step, carbohydrazide structures were obtained by reacting these hydrazide compounds with substituted benzoyl chloride in dichloromethane.

RESULTS:

The synthesized compounds were elucidated by FT-IR, 1H-NMR, 13C-NMR, HSQC, MS and their purity were checked with TLC, HPLC and elemental analysis. PARP enzyme inhibition of synthesized compounds was determined by fluorometric method. Some compounds showed significant PARP inhibition.

CONCLUSIONS:

According to activity results, compounds bearing thiomethyl substituent were demonstrated remarkable PARP inhibition among the tested compounds. Electron donating and hydrophobic groups increased the potency of activity.

Acknowledgement

This study was supported by Marmara University Scientific Research Commission [Project number: SAG-C-DRP-100616-0260].

REFERENCES:

1. Tok F, Kocyigit Kaymakcioglu B (2015). Clinical and Experimental Health Sciences. 1: 41-52.
2. Hwang SH, Wecksler AT et al. (2013). Bioorganic Medicinal & Chemistry Letters. 23:3732-3737.

P-440: SYNTHESIS OF NOVEL ANTIPYRINE DERIVATIVES AS CHOLINESTERASE INHIBITORS

[1] Tok, F., [1] Kocyigit Kaymakcioglu, B., [2,3] Saglik, BN., [2,3] Ozkay, Y.

[1] Marmara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Istanbul, Turkey

[2] Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskisehir, Turkey

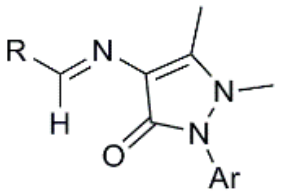
[3] Anadolu University, Faculty of Pharmacy, Doping and Narcotic Compounds Analysis Laboratory, Eskişehir, Turkey

INTRODUCTION:

Alzheimer's Disease (AD) is described as a degenerative disease of the central nervous system (CNS) and described especially by premature senile mental degradation (1). Acetylcholinesterase (AChE) is the main enzyme responsible for the hydrolysis of the ACh at the cholinergic synapses, while butyrylcholinesterase (BuChE) acts as a co-regulator of the activity of AChE. Therapeutic agents that function as inhibitors of both enzymes can ensure additional benefits in AD. Present therapies for AD mainly focus on the use of FDA accepted acetylcholinesterase inhibitors (AChEIs), i.e. donepezil, rivastigmine, galantamine, tacrine. These medications are counted as solely symptomatic. Thus, there is a need to find more efficient agents to stop the disease progression (2). The pyrazolinone ring system is significant in medicinal chemistry research because of high affinity against a variety of enzymes and protein receptors. In this study, we synthesized new compounds bearing pyrazolinone moiety and investigated their ChE inhibitory activity to gain new biologically active compounds.

MATERIALS AND METHODS:

The structure confirmation of the synthesized compounds was performed using FT-IR, 1H-NMR, 13C-NMR, and HRMS spectral data. The anticholinesterase activity assay of the synthesized compounds was performed using Ellman's spectroscopic method (3). To evaluate the binding modes of the most active compound, docking studies were performed by using Schrödinger Maestro interface (4).



Ar: Aromatic ring
R: Alkyl, aryl, halogens

RESULTS:

According to the enzyme activity studies, none of the synthesized compounds displayed significant activity on BChE enzyme. On the other hand, compounds ANT-3, ANT-6 and ANT-10 showed remarkable enzyme inhibition profile against AChE enzyme. Compound ANT-10 was the most potent derivative in the series with IC50 value of 0.0568±0.0018 μM. Also, it was carried out with the help of the docking studies that compound ANT-10 showed a notable binding capacity to enzyme active sites.

CONCLUSIONS:

Consequently, some of the synthesized compounds have been shown good inhibition profile against AChE enzyme.

REFERENCES:

1. Yeong KY, Mohamed AA et al. (2013). Bioorganic Chemistry, 49:33-39.
2. Meena P, Nemaysh V et al. (2015). Bioorganic & Medicinal Chemistry, 23:1135-1148.
3. Ellman GL, Courtney KD et al. (1961). Biochemical Pharmacology, 7:88-95.
4. Maestro, version 10.6, Schrödinger, LLC, New York, NY, 2016.

P-441: SYNTHESIS, STRUCTURAL IDENTIFICATION AND ANTICANCER EFFECTS OF NOVEL PHENOTHIAZINES FOR HEPATOCELLULAR CANCERS

[1] Zengin, F., [2,3] Yaman, M., [1] Kisla, MM., [2,3,4] Konu, O., [1] Ates Alagoz, Z.

[1]Ankara University, Department of Pharmaceutical Chemistry, Ankara, Turkey.

[2] Bilkent University, Department of Molecular Biology and Genetics, Ankara, Turkey

[3] Neuroscience Program, 4 UNAM, Ankara, Turkey

INTRODUCTION:

Phenothiazines have recently been associated with anticancer effects (1,2) however, there is a need for synthesis and structure analysis of novel phenothiazines with higher efficiency and less side effects. In this study, we designed, synthesized and structurally identified novel phenothiazine derivatives and tested their anticancer effects along with commercial phenothiazines in HCC cell lines.

MATERIALS AND METHODS:

Syntheses of the compounds were carried out starting from commercially available nonsubstitue/2-substitue-10H-phenothiazine. This was followed by reaction with chloro acetyl chloride to give 10-chloroacetylphenothiazine. The reaction of 10-chloroacetylphenothiazine with appropriate alkyl amines gave the targeted phenothiazine derivatives (3, 4). To test effects of commercial and novel phenothiazines on HCC cell lines, we used naive or GFP expressing SKHep1 and Hep3B cell lines and identified effective compounds inhibiting cell viability using MTT assays.

RESULTS:

Eight novel compounds that include different chemical groups, e.g –H, –Cl, -SCH3 at R1 and different aliphatic amines at R2, were synthesized, and structurally analyzed using 1H, 13C-NMR, Mass spectrometers. MTT assays showed that commercial phenotiazines prochlorperazine dimaleat and trifluoperazine HCl exhibited effective cell viability inhibition along with a group chemically related novel phenothiazines providing new lead molecules. Ongoing studies focus on synthesis of novel derivatives that contain -OCH3 substituted benzyl piperazine groups and will be tested in the given paradigm in SKHEP1 and HEP3B cells.

CONCLUSIONS:

In the long term, we will synthesize and test lead novel phenotiazines that can provide more effective therapies for HCC.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-116Z388) and BIDEB.

REFERENCES:

1. Gil-ad et al., (2006). Phenothiazines induce apoptosis in a B16 mouse melanoma cell line and attenuate in vivo melanoma tumor growth, 15(1):107-12.
2. Qi & Ding (2013). Potential antitumor mechanisms of phenothiazine drugs, 56(11):1020-7.
3. Nagaraja et al., (2012). Novel phenothiazine analogous: Synthesis and a new perceptivity into their antioxidant potential, 4 (3):786-794.
4. Sinha et al., (2011). Synthesis and biological activity of phenothiazine derivatives, 2 (4):1130-1137.

P-442: SYNTHESIS, BIOLOGICAL ACTIVITY AND STRUCTURAL CHARACTERIZATION OF BENZYL 4-([1,1'-BIPHENYL]-4-YL)-2-METHYL-5-OXO-1,4,5,6,7,8-HEXAHYDROQUINOLINE-3-CARBOXYLATE: A NON-MEROHEDRAL TWIN

[1] Cetin, G., [1] Simsek, R., [1] Safak, C.,[2] Yildirim Ozturk, S., [3] Butcher, RJ., [4] Wikara, J.

[1] Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry,

Ankara, Turkey

[2]Erciyes University, Faculty of Sciences Department of Physics Kayseri Turkey

[3]Howard University, Department of Chemistry Washington DC, USA

[4] University of Canterbury, School of Physical & Chemical Sciences, Christchurch NEW ZEALAND

INTRODUCTION:

1,4-dihydropyridine (1,4-DHP) derivatives were designed as calcium channel blocking compounds and then other biological activities of these compounds, including antimicrobial activity, were also investigated. The 1,4-DHP ring was converted to some other heterocyclic ring systems by condensing with various cyclic structures to obtain some derivatives have achieved both molecular diversity and more active compounds with the substitution of some aryl groups. Among these aryl groups, the compounds with biphenyl structure are notable for their high antimicrobial activity (1, 2). In view of the aforementioned findings, the condensed 1,4-DHP derivative bearing the biphenyl substituent was synthesized, the structure of the compound was proved and biological activity was investigated.

MATERIALS AND METHODS:

The compound was obtained with modified Hantzsch reaction. The structure of the compound was proved and the antibacterial and antifungal activity of the compound have been elucidated.

RESULTS:

In this study the title compound was synthesized and the structure of the compound was elucidated by using spectral methods and subjected to in vitro antibacterial and antifungal studies. The crystal structure of (I) has been determined by single crystal X-ray diffraction method (3-5). It crystallizes in orthorhombic space group Pca 21, with unit cell dimensions a = 16.9900(7), b = 10.0073(8), c = 14.0230(8) Å, V = 2384.2(3) Å3, Z = 4. This structure has been refined as a nonmerohedral twin and the nonmerohedral twin matrix has been identified.

CONCLUSION:

In this study new benzyl 4-([1,1'-biphenyl]-4-yl)-2-methyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate was synthesized and characterized by using spectral methods. The in vitro antibacterial and antifungal studies was realized.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Hacettepe University Scientific Research Projects Coordination Unit (THD-2017-13452). RJB acknowledges the NSF program (award 1205608) for funds to purchase an X-ray diffractometer.

REFERENCES:

1. Yildirim SO, Buyukmumcu Z, Butcher RJ, Cetin G, Simsek R, Safak C (2018). Journal of Molecular Structure, 1163:161-166.
2. Khanmohammadi H, Abnosi MH, Hosseinzadeh A, Erfantalab M (2008). Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 71(4):1474-1480.
3. Allen FH (2002). Acta Cryst, B58: 380–388.
4. El-Khouly A, Yıildirim SO, Butcher RJ, Simsek R, Safak C (2012). Acta Cryst., E68: 3337.
5. Yildirim S, Butcher RJ, Gunduz MG, El Khouly A, Simsek R, Safak C (2013). Acta Cryst., E69: o40–o41.

P-443: MOLECULAR DOCKING STUDIES ON DESIGNED BENZOTHIAZOLE DERIVATIVES AS K-RAS(G12C) INHIBITORS

Yenice, G., Yilmaz, S.

Trakya University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Edirne, Turkey

INTRODUCTION:

Cancer is a complex of diseases that shows itself in various tissues and cell types in people with symptoms includes numerous endogenous and exogenous carcinogenic agents and different etiologies. The common properties all these diseases share are irregular cell growth, impaired cell differentiations, tendency to metastasize, and invasiveness (1). Ras proteins a member of small GTPases family have a large variety of important roles on controlling cellular signaling pathways such as cellular growth, migration, adhesion, cytoskeletal organization, survival and differentiation (2). The mutations occur on Ras genes, causes active Ras proteins are uncontrollably proliferate and survive in tumorigenic cells. There are several therapeutic approaches proposed targeting Ras proteins in the treatment of cancer one of them is directly inhibition of Ras proteins (2). The theurapetic strategies of directly inhibiting active Ras have a difficulty in designing inhibitors to compete with the high concentrations of GTP and GDP at the nucleotide binding site due to their affinity in picomolar

range for Ras proteins (3). The mutation of position 12 glycine replaces to cysteine (mutation G12C) enables a electrophilic targeting to the mutant form but not the wild type form. The inhibitors irreversibly bind the mutant G12C Ras and stabilizes the protein in inactive GDP form (4).

MATERIALS AND METHODS:

Molecular docking calculations were performed to understand the interactions between several designed benzothiazole derivatives and K-Ras G12C (pdb: 4L8G) enzyme, by using CDocker method in Accelerys Discovery Studio 3.5 software (5).

RESULTS:

Binding properties of benzothiazole derivatives were investigated and it was found that Tyr32, Thr35 and Gly60 amino acids were playing an important role for enzyme-ligand interactions and compounds were bound to enzyme with -71,89 to -34,39 kcal/mol binding energies.

CONCLUSIONS:

With the results of the study, it is inevitable that, the strategy on mutation-selective inhibitors will be the important milestone in the mutation-specific anti-Ras treatments.

REFERENCES:

1. William BC, Gregory JT (2017) The Molecular Basis of Human Cancer, 2nd ed. pp:1-24
2. Takashima A, Faller DV (2013) Expert Opin Ther Targets. 17(5):507–531.
3. John J, Rensland H, et al., (1993). J Biol Chem. 268:923–929.
4. Marín-Ramos NI, Ortega Gutiérrez S, et al., (2018). Seminars in Cancer Biology. in press.
5. Accelrys, Discovery Studio v3.5. (2012).

P-444: STRUCTURAL ELUCIDATION OF SOME CINICALLY USED KINASE INHIBITORS BY 2D ROESY NMR SPECTRA

[1] Karaaslan, C., [2] Goker, H.,

[1] Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Ankara University,

[2] Central Instrumental Analysis Laboratory, Faculty of Pharmacy, Ankara University

INTRODUCTION:

Erlotinib HCl and Gefitinib (4-aminophenylquinazoline derivatives) are anticancer agents that act as a protein kinase inhibitors for epidermal growth factor receptor (EGFR) associated tyrosine kinase. They are both used in the treatment of chemoresistant Non-Small Cell Lung Cancer (NSCLC) and Erlotinib has been reported to be effective in the treatment of several other types of cancer as well. There is a complexity about the previously published NMR data of Erlotinib and its HCl salt.

MATERIALS AND METHODS:

In this work, total structural assignments of Erlotinib, Erlotinib HCl and Gefitinib have been achieved by using 2D-NMR experiments. 2D NMR data of Erlotinib, Erlotinib HCl and Gefitinib have been performed by a detailed 2D NMR study using COSY, DEPT, 1H-13C correlated HSQC and HMBC, and ROESY methods, leading to a full 1H and 13C signals assignments.

RESULTS:

ROESY experiment gives the best important data for their structural elucidation. In addition, virtual 3D conformational data of Erlotinib and Gefitinib also support these findings.

CONCLUSIONS:

Total structural assignments of Erlotinib, Erlotinib HCl and Gefitinib have been achieved by using 2D-NMR experiments, including DEPT, COSY, ROESY, HSQC and HMBC.

ROESY experiment gives the best important data for their structural elucidation.

ACKNOWLEDGEMENTS:

Central Laboratory of Pharmacy Faculty of Ankara University provided support for the acquisition of the NMR and mass spectrometer used in this work. We thanks for providing Erlotinib HCl and Gefitinib to ATABAY Pharmaceuticals And Fine Chemicals Inc.

P-445: SYNTHESIS OF CONDENSED 1,4-DIHYDROPYRIDINE DERIVATIVES AND THEIR EFFECTS ON L-/T-TYPE CALCIUM CHANNELS.

[1] Aygun, H., [2] Zhang, FX., [2] Zamponi, GW.,[1] Gunduz, MG.

[1] Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

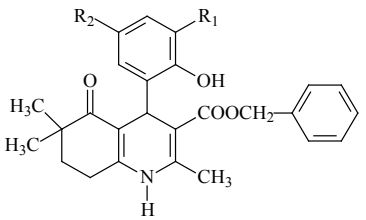
[2] University of Calgary, Hotchkiss Brain Institute and Alberta Children's Hospital Research Institute, Department of Physiology and Pharmacology, Calgary, Canada

INTRODUCTION:

1,4-Dihydropyridines (1,4-DHPs) interact at a specific class of voltage-gated calcium channel to produce their cardiovascular effects and are used to treat conditions such as hypertension and angina (1). Although their primary target in the cardiovascular system is the L-type calcium channel isoform, however, a number of 1,4-DHPs also block different kinds of calcium channels, mainly low-voltage-activated T-type calcium channels (2). In the present study, we synthesized eight 1,4-DHP derivatives in which substituted cyclohexane rings are fused to the DHP ring, and determined how different substituents on the phenyl ring affect L- and T-type calcium channel block.

MATERIALS AND METHODS:

The general procedure for the synthesis of 1,4-DHP derivatives was as follows: 4,4-dimethyl-1,3-cyclohexanedione, substituted benzaldehyde, benzyl acetoacetate and ammonium acetate were subjected to microwave irradiation in absolute ethanol. Calcium channel blocking effects of these compounds were determined on L-type (Cav1.2) and T-type (Cav3.2) calcium channels.



R_1, R_2: H, Cl, NO_2, Br

RESULTS:

The obtained results indicated that the synthesized compounds produced moderate blocking effects on both L- and T-type calcium channels. Only compound 8 blocked T-type calcium channel very effectively. As the only difference between the compounds is their substituents on C-4 phenyl ring, this suggests that types of the substituents on the aromatic ring play a key role in the ability of these compounds to block calcium current.

CONCLUSIONS:

In this study, eight condensed 1,4-DHP (hexahydroquinoline) derivatives were achieved via a modified Hantzsch reaction and their effects on L-/T-type calcium channels were reported. Compound 8, bearing two nitro groups on the phenyl ring, was found to block T-type calcium channel selectively. Our data reveal that this compound can be used for pain therapies.

REFERENCES:

6. Zamponi GW, Striessnig J, Koschak A, Dolphin AC (2015). Pharmacological Reviews, 67:821-870.
7. Bladen C, Gadotti VM, Gunduz MG, Berger ND, Simsek R, Safak C, Zamponi GW, 2015, 467:1237–1247.

P-446: ANTI-BACTERIAL AND ANTI-FUNGAL PROPERTIES OF INDOLE-HYDRAZONE DERIVATIVES

[1] Shirinzadeh, H., [2] Altanlar, N., [3] Suzen, S

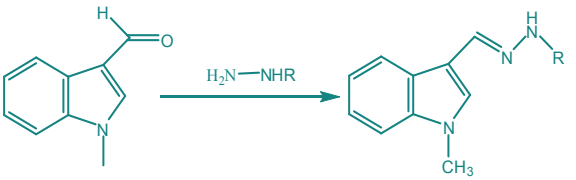
[1] Erzincan University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry,Erzincan,Turkey

[2] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Ankara, Turkey

[3] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

INTRODUCTION:

Indoles and hydrazone-type molecules establish significant classes of pharmacologically active agents against especially multi-drug-resistant microbial infections. This presented research represent the anti-bacterial and anti-fungal activity results of 1-methylindole-3-carboxaldehyde hydrazone derivatives (1, 2).



MATERIALS AND METHODS:

These derivatives were tested for their in vitro antimicrobial activities using the two-fold serial dilution technique against Staphylococcus aureus, methicillin-resistant S. aureus, methicillin-resistant S. aureus isolate, Escherichia coli, Bacillus subtilis, and Candida albicans. The minimum inhibitory concentration (MIC) was determined for the test compounds and for the reference standards sultamicillin, ampicillin, fluconazole and ciprofloxacin (3).

RESULTS:

All tested molecules showed a broad spectrum of activity having MIC values of 6.25–100 µg/ml against the tested microorganisms. Aromaticity and side chain as well as the halogens of the phenyl ring with especially fluorine and chlorine atoms were found to be noteworthy for the antimicrobial activity.

CONCLUSIONS:

These results found promising for further antimicrobial research on melatonin analogue compounds.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (109S099)

REFERENCES:

1. Karali N, Gursoy A, Kandemirli F, Shvets N, Kaynak FB, Ozbey S, Kovalishyn, V, Dimogloc A(2007). Bioorg. Med. Chem, 15:5888-5904.

2. Bektas H¸ Demirbas A¸ Demirbas N, Karaoglu SA (2010). Turk. J. Chem, 34:165–180.
3. Charles ES, Agrawal VK, Sharma S, Iyer RN (1979). Eur. J. Med. Chem. Chim. Ther, 14:435 – 438.

P-447: ANTIOXIDANT PROPERTIES OF NEW MELATONIN ANALOGUES: SYNTHESIS AND IN VITRO BIOLOGICAL ACTIVITY STUDIES

[1] Shirinzadeh, H., [2] Karaaslan, C., [3] Eren, B., [3] Gurer Orhan, H., [2] Suzen, S

[1]Erzincan University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Erzincan, Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

[3]Ege University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Izmir, Turkey

INTRODUCTION:

Oxidative stress, defined as a disturbance in the balance between the production of free radicals and antioxidant defenses which results in terminal macromolecular damage and related diseases (1, 2). Antioxidants are molecules that can neutralize free radicals by accepting or donating electrons to eliminate the unpaired condition of the radical before important and essential molecules are damaged. The aim of this study was to synthesize and examine possible in vitro antioxidant effects of indole-based melatonin analogue compounds (3).

MATERIALS AND METHODS:

As a part of our ongoing study twenty one indole hydrazide/hydrazone derivatives were synthesized, characterized and their in vitro antioxidant activity was investigated (4). The synthesized compounds were tested for their antioxidant activities using Antioxidant effects on ROS-induced DCFH-DA oxidation and Membrane stabilizing effect; LDH leakage.

RESULTS:

Almost all compounds were found to exhibit higher antioxidant activity when they are challenged with H2O2. N methylation of the indole ring decreased the antioxidant capacity of all MLT derivatives. We determined LDH activity in the culture medium in order to assess the membrane stabilizing effect of MLT analogues. No increases in LDH activity were observed with any of the tested compounds. Several compounds were found to decrease LDH leakage indicating membrane stabilizing effect.

CONCLUSIONS:

Antioxidants protect cells from damage caused by unstable molecules known as free radicals. These results found promising for further research on the synthesis of antioxidant activity studies of melatonin analogue compounds.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (109S099 and 108S202)

REFERENCES

1. Bonnefont Rousselot D, Collin F (2010). Toxicology. 278:55–67.
2. Tan D.X, Chen L.D, Poeggeler B, Manchester LC, Reiter RJ (1993). Endocr. J. 1:57–60.
3. Singh R.P, Sharad S, Kapur SJ (2004). Ind Acad Clin Med.4:218–225.
4. Kidwai M, Negi N, Gupta SD (1994). Chem Pharm Bull. 42:2363–2364.

P-448: MOLECULAR DOCKING STUDIES, SYNTHESIS AND DETERMINATION OF ACHE/BCHE INHIBITION OF NEW HYDRAZONE DERIVATES

[1] Bozbey, I., [1] Uslu, H., [2] Senol, FS.

[1] Inonu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Malatya, Turkey

[2] Gazi University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

Alzheimer's disease (AD) is a chronic progressive neurodegenerative disorder. It is connected with a selective loss of cholinergic neurons, which occurs due to various neuropathological conditions (1). Two important enzymes from the group of serine hydrolases, acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) are usually defined as cholinesterases (ChEs). The major role of AChE is to catalyse the hydrolysis of acetylcholine (ACh) in cholinergic synapses, whereas the function of BChE is less clearly defined because it can hydrolyse ACh as well as other esters (2-3). A series of hydrazone derivatives were designed, synthesized, and their inhibitory effects on acetylcholinesterase and butyrylcholinesterase were evaluated in pursuit of potent dual inhibitors.

MATERIALS AND METHODS:

We synthesized the compounds by the reaction of hydrazone derivates according to literature (4). We determined their anticholinesterase activities according to the Ellman's method. 4EY7 pdb file with resolution 2.3509Å and 4BDS pdb file with resolution 2.1Å were received (www.rcsb.org) and were modified using the ADT package version 1.5.6rc3. To validate the docking program, the co-crystallized ligands Donepezil (PDB ID:E20) and Tacrin (PDB ID:THA) were redocked on the target enzymes.

RESULTS:

It was understood that the synthesized compounds have more potent inhibitory activity against BChE enzyme compared to AChE enzyme. Compound C11 was the most active compound against BChE with 89.43±1.94% inhibition potency at 10-6M concentration and IC50 value of 4.27±0.36μM. Most of the compounds showed BChE inhibition at very low concentrations according to reference drug. Molecular modeling studies indicated that compounds bind to AChE and BChE enzymes in a similar position with co-crystals.

CONCLUSIONS:

In the present study, cholinesterase inhibitory potency of some novel hydrazone derivatives was investigated. Compound C11 was found as the most active compound aganist BChE. None of the compounds showed AChE activity as much as standard drug Galantamine HBr. Otherwise, methoxy substitutions on phenyl ring positively affected cholinesterase activity.

REFERENCES:

1. Kwon YE et al., (2007). J.Y.Bioorg. Med. Chem., 15, 6596-6607
2. Groner E et al., (2007). M.Mol. Pharmacol., 71, 1610.
3. Chiou SY, Huang CF, Hwang MT, (2009). Lin, G.Mol. Toxicol., 23, 303.
4. Özdemir Z et al., (2016). Med Chem Res., 26: 2293–2308

P-449: IN VITRO ANTICANCER ACTIVITY OF NEW NAPHTHYL ETHANONE OXIME ESTER DERIVATIVES BEARING PYRAZOLE MOIETY

[1] Bozbey, I., [1] Uslu, H., [2] Salva, E., [1] Karakurt, A.

[1] Inonu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Malatya, Turkey

[2] Inonu University, Faculty of Pharmacy, Department of Pharmaceutical Biotechnology, Malatya, Turkey

INTRODUCTION:

Cancer is a major health problem that causes deaths worldwide (1) and a fatal disease characterized by uncontrolled cell proliferation, invasive characterization and metastasis (2). There are intensive studies in chemotherapy fields in order to develop effective compounds against cancer cells. Heterocyclic compounds are frequently used in medicinal chemistry, especially in the development of active biological compounds (3). For this, we designed oxime ester derivative compounds containing the pyrazole ring. Also, the ketone group in the main structure was replaced by alcohol and oxime groups which are bioisosters of this group. The ester derivatives of the oxime groups have been synthesized to obtain more lipophilic compounds. The in vitro cytotoxic activity was evaluated for all of the synthesized compounds against the SH-SY5Y cell lines.

MATERIALS AND METHODS:

Their structures were determined by 1H-NMR, 13C-NMR, elemental analyses and mass spectrum. 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay was performed to determine effect of the formulations on cell viability. Measurements were performed at 48th hours. The color density was measured in 570 nm with a multiwell Elisa Platten reader. Results were evaluated using cell viability (%) parameter.

RESULTS:

Cell viability values for the compounds were found in the range of 65.99-105.94 %. Compound d3 is the most active compound with a value of 65.99%.

CONCLUSIONS:

Most of the compounds showed moderate to high activity with cell viability values. It is considered that the alkyl substitution of the R group increases the activity.

REFERENCES:

1. Zheng LW et al., (2010). Bioorg. Med. Chem. Lett, 20:4766-70.
2. Pérez-Herrero E, Fernández-Medarde A (2015). Eur J Pharm Biopharm, 93:52-79.
3. Neochoritis C, Tsoleridis CA, Stephanidou-Stephanatou (2008). Tetrahedron,64: 3527-33.

P-450: MODIFICATION OF MALEIC ANHYDRIDE-ALT-ACRYLIC ACID COPOLYMER AS A POTENTIAL ANTICANCER AND ANTIBACTERIAL ACTIVE CONJUGATES

[1] Karakus, G., [2] Kaplan Can, H., [3] Sahin Yaglioglu, A.

[1]Cumhuriyet University, Faculty of Pharmacy, Pharmaceutical Chemistry Department, Sivas, Turkey

[2]Hacettepe University, Faculty of Science, Department of Chemistry, Ankara, Turkey

[3]Cankiri Karatekin University, Faculty of Science, Chemistry Department, Cankiri, Turkey

INTRODUCTION:

Water-soluble polymer have been designed as drug carrier with biologically active agents that can be attacked by amino (-NH2) or hydroxyl groups (-OH) of nucleophilic reagents (1). Acriflavine (AF) has an anticancer activity and used in AIDS treatments (2). Hydroxyurea (HX) is an antineoplastic agent that has antiretroviral properties in (HIV/AIDS) with limited use due to its many side effects depending on its cytotoxicity on tissues (3).

MATERIALS AND METHODS:

Maleic anhydride-alt-acrylic acid (MAAA) were conjugated with AF and HX by ring opening reaction or anticancer and antibacterial active conjugates in N,N-dimethylformamide (DMF), 48 h, using triethylamine (TEA) as the catalyst, at 70 °C for MAAA/AF and 75 ºC for MAAA/HX. Structural characterization was performed by Fourier Transform Infrared Spectroscopy (FTIR) and Proton Nuclear Magnetic Resonance Spectroscopy (1H-NMR). Physical characterization of MAAA/HX was performed by Thermogravimetric Analysis (TGA) and Differential Scanning Calorimetry (DSC). Previously, Antimicrobial activity of the MAAA/AF was evaluated by Kirby Bauer Disc Diffusion method using four different strains. Antiproliferative activity of MAAA/HX was performed by BrdU cell proliferation ELISA assay on C6 (rat brain tumor) and HeLa (human cervix carcinoma) (4).

RESULTS:

MAAA/AF had antibacterial activity on EHEC (Enterohaemorrhagic Escherichia coli) and S. aureus (5). MAAA/HX significant antiproliferative activity against C6 and HeLa, increased antitumor activity and also decreased toxicitycompared to crude drug.

CONCLUSIONS:

Activity test results confirmed that conjugation reaction of MAAA performed via ring-opening reactions (4). In our previous study drug carrier MAAA copolymer conjugated for antibacterially active MAAA/AF, in this study it is especially suggested for MAAA/HX conjugate having highly antiproliferative activity.

REFERENCES

1. Saad GR, Morsi RE, Mohammady SZ, Elsabee MZ (2008). Journal of Polymer Research, 15:115-123.
2. Eldaroti HH, Gadir SA, Refat, Adam AMA (2013). International Journal of Electrochemical Science, 8:5774–5800.
3. Liebelt E, Balk S,Faber W, Fisher J, Hughes C, Lanzkron S, Lewis K, Marchetti F, Mehendale H, Rogers JM, Shad AT, Skalko RG, Stanek EJ (2007). *Birth Defects Research* Part *B* Developmental and *Reproductive* Toxicology, 80:259–66.
4. Karakus, G, Polat ZA, Sahin Yaglioglu A, Karahan M, Yenidunya AF (2013). Journal of Biomaterials Science, Polymer Edition, 24:1260-1276.
5. Kaplan-Can H, Karakus G and Tuzcu N (2014). Polymer Bulletin, 71:2903–2921.

P-451: SYNTHESIS AND MOLECULAR DOCKING STUDIES OF NOVEL HYDRAZONES BASED ON BENZOXAZOLINE SCAFFOLD AS SELECTIVE MAO-B INHIBITORS.

[1] Tasci, H., [2] Saglik, BN., [2] Ozkay, Y., [1] Tozkoparan, B., [1] Gokhan Kelekci, N.

[1] Hacettepe University, Faculty of Pharmacy Dept of Pharmaceutical Chemistry, Ankara-Turkey

[2] Anadolu University, Faculty of Pharmacy Dept of Pharmaceutical Chemistry, Eskişehir-Turkey

INTRODUCTION:

Monoamine oxidases (MAOs) that belong to the family of flavin-containing amine oxidoreductases and catalyze the oxidative deamination of monoamines as serotonin, dopamine, histamine. Subtypes of MAO are MAO-A and MAO-B were distinguished by their substrate and inhibitor specificity (1). Increased oxidative stress and decreased antioxidative protection that is a result of oxidation activity of MAOs, are important causes of neurodegeneration which play a role in the pathophysiology of several neuropsychiatric disorders as depression, Alzheimer's disease (AD), and Parkinson's disease (PD). Therefore MAO inhibition is thought drug target for therapy of these diseases and disorders (2). It has been reported that hydrazone and acylhydrazone derivatives exhibits anticonvulsant, antiinflammatory, antidepressant, analgesic, antithrombocyte and anti-cancer activities. There have been also many reports on the antidepresant/MAO-inhibition activity of hydrazones derived from substituted hydrazides and their reduction products (3). In this study, the synthesis of some new substituted benzoxazolinehydrazones (figure 1) were aimed to reach more potent MAO inhibitory compunds. These derivatives were synthesized by reacting 5-substitutedbenzoxazolinone-3-carboxylic acid hydrazide with various aldehydes, their structures were confirmed using IR, 1H-NMR, mass and elemental analysis. The compounds were investigated for their ability to inhibit hMAO isoforms by in-vitro tests. Molecular docking studies were done to provide insights into enzyme-inhibitor interactions and a rationale for the observed inhibition towards monoamine oxidases.

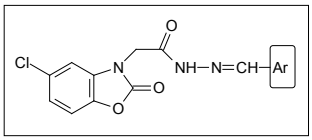


Figure 1. General structure of new substituted benzoxazolinehydrazones

RESULTS:

All of the designed compounds have exhibited good inhibitory efficacy against hMAO-B.

CONCLUSIONS:

In comparison with our previous study, although the electron withdrawing groups in aromatic aldehyde ring that used in hydrazone synthesis generally have a positive effect on the MAO inhibition activity, electron donating groups as ethyl were found to have a higher contrubution to the MAO inhibition potential of these derivatives.

ACKNOWLEDGEMENT

This study was supported by Hacettepe University Scientific Research Projects Coordination Unit (THD-2018-16821).

REFERENCES :

1. Fowler, CJ, Tipton, KF (1984). J. Pharm. Pharmacol., 36(2): 111-115.
2. Youdim, MBH, Weinstock, M (2004). Neurotoxicology, 25(1-2): 243-250.
3. Salgin-Goksen, U., et al., (2013). J. Neural Transm.,120(6):883-891.
4. Milcent R et al., (1996). J. Heterocycl. Chem. 33:1829–1833.
5. Salgin-Goksen U et al., (2007). Bioorg Med Chem 15:5738–5751.

P-452: SYNTHESIS, CHARACTERIZATION AND PHARMACOLOGICAL STUDIES OF SOME NEW MANNICH BASES DERIVED FROM 1,2,4-TRIAZOLES

[1] Avci, A., [1] Tasci, H., [1] Gokhan Kelekci, N., [2] Aztopal, N., [2] Ulukaya,E., [1] Tozkoparan, B.

[1]Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

[2]Istinye University, Molecular Cancer Research Center, Istanbul, Turkey

INTRODUCTION:

Classical Mannich reaction is a way for the introduction of aminomethyl function into the molecules. Mannich bases can be classified into four main categories according to the atom involving aminoalkylation reaction: C-Mannich bases (ketonic mannich bases, phenolic mannich bases, alkyne mannich bases etc.), N-Mannich bases (amide mannich bases, sylfonamide mannich bases etc.), S-Mannich bases (mannich bases of thiophenols), P-Mannich bases (mannich bases of dialkyl phoshites). These derivatives represent a class of synthetic compounds with a wide spectrum of biological activities. Many type of Mannich derivatives have been reported to have high activity against certain cancer types through variable pathways (1). Due to the increasing prevalence of cancer with resistance against existing chemotherapeutics, discovery of new molecules in this area is still a challenging topic. 1,2,4-Triazole is one of the important core fragments which is incorporated in some anticancer drugs such as anastrozole, letrozol etc. Therefore 1,2,4-triazole ring constituted our starting point to generate novel N-Mannich bases as putative anticancer agents.

MATERIALS AND METHODS:

The synthesis of target compounds were performed via the classical Mannich reaction, a one-pot three component condensation reaction, by reacting triazole molecule, formaldehyde and diverse secondary amines in ethanole (2). The structures of the compounds were confirmed by both spectroscopic and elemental analysis. For initial screening, the cytotoxic activity against four different cancers and a normal cell line was measured by SRB assay using the compounds at the concentration of 10 microMolar. The selected compounds at a broad range of concentrations were further evaluated by ATP viability assay to calculate the IC50 values.

RESULTS:

Pharmacological studies of the compounds are under investigation. The results will be discussed in the poster.

REFERENCES:

1. Roman G (2015). European Journal of Medicinal Chemistry 89:743-816.
2. Tozkoparan B et al., (2005). Arzneimittel Forschung - Drug Research. 55(9):533.

P-453: SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF TRIFLOUROMETHYL ACETOPHENONE OXIME ESTER DERIVATIVES

[1] Bozbey, I., [2] Kart, D., [1] Karakurt, A.

[1] Inonu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Malatya, Turkey

[2] Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Ankara, Turkey

INTRODUCTION:

Infectious diseases remain a great health problem throughout the world. Although there are several drugs in the market, there is an emerging crisis of antimicrobial resistance for microbial pathogens (1,2). The evolution rate of bacterial resistance to antibiotics is evidently higher than the development rate for new classes of antibiotics. Thus, new drug needs are increasing. In this study a new series of oxime ester were synthesized and evaluated for their antibacterial activity towards S. aureus (ATCC 29213), P. aeruginosa (ATCC 27853), E. faecalis (ATCC 29212), E. coli (ATCC25922) species.

MATERIALS AND METHODS:

We synthesized the final compounds by the reaction of oxime derivate (d) with various acyl chlorides using 4-dimethylaminopyridine. Then, c was converted to its oxime derivate (d) by refluxing with NH2OH. HCl under alkali conditions. Acetophenone derivate (b) was converted to the ketones by N-alkylation of 1H-imidazole. We prepared b by brominating a. Their structures were determined by 1H-NMR, 13C-NMR, elemental analyses and mass spectral. All newly synthesized compounds were screened for their antibacterial activities against laboratory strains by using microdilution method.

RESULTS:

The antibacterial activity results indicate that all compounds were more effective against the Gram-(+) bacteria than the Gram-(-) bacteria. Most of the compounds showed moderate to high activity with MIC values in the range of 4-512 µg/mL.

CONCLUSIONS:

The objective of this work was to design and synthesize new compounds with antibacterial properties. Compound 2, 4 and 5 have good antibacterial activity against S.aureus and P.aeruginosa. p-Substituted benzene groups showed better activity and the alkyl substitution of the R group increased activity.

ACKNOWLEDGEMENTS:

This study was supported by a grant of INU-BAP (2017/803)

REFERENCES:

1. Alanis AJ et al., (2005). Arch. Med. Res. 36(6), 697-705.
2. Sharma PK et al., (2011). Eur J Med Chem2011; 46: 1425-32.

P-454: CYTOTOXIC EFFECTS OF NEW TRIFLOUROMETHYL OXIME ESTER COMPOUNDS BEARING IMIDAZOLE MOIETY ON NEUROBLASTOMA CELL LINE

[1] Bozbey, I., [2] Salva, E., [1] Karakurt, A.

[1] Inonu University, Faculty of Pharmacy,Department of Pharmaceutical Chemistry, Malatya, Turkey

[2] Inonu University, Faculty of Pharmacy, Department of Pharmaceutical Biotechnology, Malatya, Turkey

INTRODUCTION:

Neuroblastoma is a tumor that occurs in the adrenal medulla and sympathetic ganglia, originating from primitive neural crest cells. It is also the most common extracranial solid tumor and is responsible for 8-10% of all childhood malignancies. There are about 800 new patients per year in the US (1). It is thought that about 22% of all neuroblastoma patients have germinal mutation (2). The aim of this study was to investigate the cytotoxic effects of new oxime ester compounds on SH-SY5Y neuroblastoma cells.

MATERIALS AND METHODS:

The structures of the compounds were confirmed by IR, 1H-NMR, 13C-NMR, and elemental analyses. Cell viability was assessed with 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. Neuroblastoma cells were cultured in appropriate culture medium. They were transferred to 96-well plates and were incubated at 48 hours. Paclitaxel was used as a positive control. The color density was measured in 570 nm with a multiwell Elisa Platten reader. Results were determined using cell viability (%) parameter.

RESULTS:

The cell viability values of the compounds were in the range of 51.02-65.37%. The activity results showed that compound (E/Z)-1-(4-trifluoromethylphenyl)-2-(1H-imidazol-1-yl)ethanone O-4-trifluoromethylbenzoyl oxime is the most active derivative in the series. Cell viability values of the ketone (1-(4-trifluoromethylphenyl)-2-(1H-imidazol-1-yl)ethanone), alcohol (1-(4-trifluoromethylphenyl)-2-(1H-imidazol-1-yl)ethanol) and oxime (1-(4-trifluoromethylphenyl)-2-(1H-imidazol-1-yl) etanone oxime) compounds were 73.153%, 76.491%, 65.528%, respectively.

CONCLUSIONS:

It is considered that the presence of alkyl groups in the ester moiety of the compound increased the effect. The ketone, alcohol and oxime structures showed good activity.

ACKNOWLEDGEMENTS:

This study was supported by a grant of INU-BAP (2017/803)

REFERENCES:

1. Gurney JG et al., (1997). J Pediatr Hematol Oncol., 19:428-32.
2. Olshan AF, Smith J, Cook MN, et al., (1999). Am J Epidemiol, 150:930-8.

P-455: SYNTHESIS OF SOME 1H-BENZIMIDAZOLE COMPOUNDS BEARING BIS-THIOSEMICARBAZIDE AND TRIAZOLE DERIVATIVES AS INHIBITORS OF EGFR TYROSINE KINASE

[1] Celik, I., [1] Ayhan Kilcigil, G., [2] Guven, B., [2] Kara, Z., [2] Onay Besikci, A.

[1] Ankara University, Department of Pharmaceutical Chemistry, Ankara, Turkey

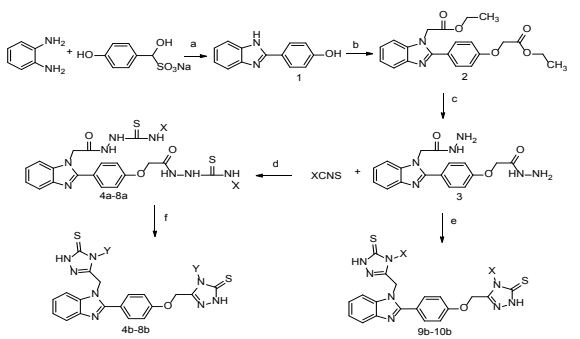
[2] Ankara University, Department of Pharmacology, Ankara, Turkey

INTRODUCTION:

EGFR kinases are being high rate expression in a lot of cancer types, particularly in lung and breast cancer. In that cancer types are highly expressed more rate %40-80 EGFR according to normal cell (1). Benzimidazole derivatives have been found as anticancer inhibitors including tyrosine kinases (2-4).

MATERIALS AND METHODS:

Thiosemicarbazides were obtained by condensing acyl hydrazides with the methyl, ethyl, propyl, phenethyl and cyclohexyl isothiocyanates in ethanol-DMF mixture (1:1). Triazoles were synthesized from that thiosemicarbazides (3.4 mmol) in 10 ml 1 N NaOH by refluxing for 1 h (4b-8b)/ from the reaction of hydrazides with 2-piperidinoethyl or 2-(4-morpholino) ethyl isothiocyanate in DMF (9b-10b). Following the structure elucidation (1H NMR, 13C NMR, MS), benzimidazole compounds bearing bis-thiosemicarbazide and bis-triazole were tested for their EGFR kinase inhibitory activities. ADP-Glo™ kinase assay determines kinase activity based on the quantification of the amount of ADP produced during a kinase reaction.



Synthetic route for the preparation of compounds **4a-8a** and **4b-10b**. Reagents: (a) $Na_2S_2O_5$; (b) $ClCH_2COOEt$/KOH-DMSO; (c) $NH_2NH_2{\cdot}H_2O$/EtOH; (d) methyl, ethyl, propyl,cyclohexyl, phenethyl; (e) 2-piperidinoethyl, 2-(4-morpholino)ethyl isothiocyanate; (f) NaOH

RESULT:

We measured the activity of EGFR kinase and evaluated the inhibitory efficiencies of the benzimidazole compounds bearing bis-thiosemicarbazide and bis-triazole ring by comparing them with erlotinib.

Conclusions:In this study, a series of new benzimidazole derivatives 4a–8a and 4b–10b having bis-thiosemicarbazide and bis-triazole synthesized, and their anti-EGFR kinases activities were evaluated. In summary, promising results were obtained for further studies.

REFERENCES:

1. Yewale C, Baradia D, Vhora I, Patil S, Misra A (2013). Biomaterials**,** 34(34):8690-8707.
2. Chu B, Liu F, Li L, Ding C, Chen K, Sun Q, Shen Z, Tan Y, Tan C, Jiang Y (2016). Cell death & disease. 6 (3):e1686.
3. Li Y, Tan C, Gao C, Zhang C, Luan X, Chen X, Liu H, Chen Y, Jiang Y (2011). Bioorganic & medicinal chemistry. 19(15):4529-4535.
4. Yadav S, Sinha D, Singh SK, Singh VK (2012). Chemical biology & drug design**.** 80 (4):625-630.

P-456: SYNTHESIS OF SOME CYCLOHEXYL SUBSTITUTED OXADIAZOLE DERIVATIVES LINKED 1H-BENZIMIDAZOLE

Celik, I., Ayhan Kilcigil, G.

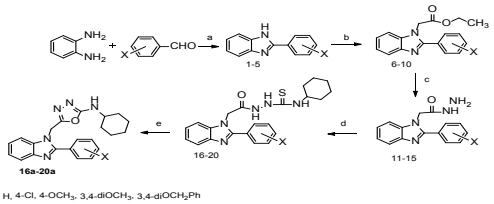
Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

INTRODUCTION:

Recently, the oxadiazole and benzimidazole rings in heterocyclic compounds have attracted many medicinal chemists and other researchers. Compounds including 1,3,4-oxadiazole and 1H-benzimidazole have a lot of pharmaceutical activity as antimicrobial, antifungal, anticancer, anti-inflammatory, anticonvulsant, antioxidant, antiviral, antiulcer, antiangiogenic and antiproliferative effects etc. For this reason, we are synthesized new oxadiazole linked benzimidazole compounds (1-3).

MATERIALS AND METHODS:

For the target compounds, the reaction sequences are summarized in Scheme1. Firstly, 2-phenyl/substitutedphenyl-1H-Benzo[d]imidazole was prepared via oxidative condensation of o-phenylenediamine, benzaldehyde and sodium metabisulfite. Reaction of the benzimidazole compound with ethyl chloroacetate gave the ethyl 2-(2-substitutedphenyl)-1H-benzo[d]imidazol-l-yl) acetate derivatives (6-10). Hydrazine hydrate and the esters (6-10) in ethanol were refluxed for 4 h to give 2-(2-phenyl/substitutedphenyl)-1H-benzo[d]imidazol-l-yl)acetohydrazides (11-15). Thiosemicarbazides (16-20) were obtained by condensing acyl hydrazides with the cyclohexylisothiocyanate in ethanol. Oxadiazoles were synthesized from that thiosemicarbazides (0.5 mmol) in 1 ml DMSO by refluxing for 4 h at 140 0C (4). All synthesized molecules were crystallized from ethanol or acetone/water (3:1) and melting point was revealed. NMR and Mass spectral analysis were performed at Ankara University, Faculty of Pharmacy.



X: H, 4-Cl, 4-OCH_3, 3,4-diOCH_3, 3,4-diOCH_2Ph

Synthetic route for the preparation of compounds **16a-20a**. Reagents: (a) $Na_2S_2O_5$; (b) $ClCH_2COOEt$/KOH-DMSO; (c) $NH_2NH_2{\cdot}H_2O$/EtOH; (d) cyclohexyl isothiocyanate; (e) DMSO

RESULTS:

The mass spectra of synthesized compounds showed a M+H ion peak, which is confirming with the molecular formula of the compounds. In the NMR spectral data, all protons were seen according to the expected chemical shift and integral values.

CONCLUSIONS:

The structures of the synthesized compounds were consistent with the 1H, 13C-NMR, and mass spectra.

REFERENCES:

1. Ayhan Kilcigil G, Kus C, Ozdamar ED, Can-Eke B (2007). Iscan, M., Archiv der Pharmazie. 340 (11):607-611.
2. Keri RS, Hiremathad A, Budagumpi S, Nagaraja B (2015). Chemical biology & drug design**.** 86 (1):19-65.
3. Vaidya A, Jain S, Jain P, Jain P, Tiwari N, Jain R, Jain R, K Jain A, K Agrawal R (2016). Mini reviews in medicinal chemistry**.** 16(10):825-845.
4. Bao W, Chen C, Yi N, Jiang J, Zeng Z, Deng W, Peng Z, Xiang (2017). Chinese Journal of Chemistry**.** 35(10):1611-1618.

P-457: SYNTHESIS AND ANTICANCER ACTIVITY OF NEW (S)-NAPROXEN DERIVATIVES AS METHIONINE AMINOPEPTIDASE (TYPE II) INHIBITORS

[1,2] Birgul, K., [3] Uba, AI., [4] Bekci, H., [4] Cumaoglu, A., [5] Yilmaz, O., [3] Yelekci, K., [1] Kucukguzel, SG.,

1 Marmara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Haydarpasa 34668 Istanbul, Turkey

[2] Altınbaş University, Faculty of Pharmacy, Department of.Pharmaceutical Chemistry, Istanbul, Turkey

[3]Kadir Has University, Faculty of Engineering and Natural Sciences, Department of Genetics and Bioengineering, 34083 İstanbul, Turkey

[4] Erciyes University, Faculty of Pharmacy, Department of Biochemistry, Kayseri, Turkey

[5] TUBITAK Marmara Research Center, Kocaeli, Turkey

INTRODUCTION:

Naproxen (S)-2-(6-methoxy-2-naphthyl)propanoic acid is a non-steroidal anti-inflammatory drug (NSAID) reported to be which is anticancer effect in the literature (1). Anticancer activity of thiosemicarbazides (2), 1,2,4-triazoles-3-thiones (3) and thioethers (4) have been reported in literatures. In the light of these literatures, we synthesized and studied anticancer effects of new naproxen derivatives on prostat cancer cell lines PC-3, DU-145 and LNCaP.

MATERIALS AND METHODS:

The naproxen ester (methyl (S)-2-(6-methoxynaphthalen-2-yl) propanoate) [1] and naproxen hydrazide ((S)-2-(6-methoxynaphtalen-2-yl)propanoic acid hydrazide) [2] were prepared according to the literature method (5).Compound 2 and substitutedphenylisothiocyanate refluxed to form new (S)-2-(2-(6-methoxynaphthalen-2-yl) propanoyl-N-arylthiosemicarbazide [3]. The naproxen thiosemicarbazides reacted with 4N NaOH solution and obtained (S)-5-(1-(6-methoxynaphthalen-2-yl)ethyl)-4-substitued-1,2,4-triazole-3-thiol [4]. In addition, naproxen thioethers ((S)-3-(substituedbenzylthio)-5-(1-(6-methoxynaphthalen-2-yl)ethyl)-4-substituted-1,2,4-triazoles) [5a-h] were synthesized by the reaction of compound 4 and substitued benzyl chloride with the presence of potassium carbonate in ethanolic medium.

RESULTS:

The aim of this study is synthesize and study anticancer activity of new naproxen derivatives [3,5a-h] which structures were identified by FT-IR, 1H-NMR and impurity profiles were controlled by elemental analysis and TLC. Compounds 5b (6) and 5h showed the most potent anticancer activity against PC-3 cell line (IC50 = 34.7 µM, 16.3 µM, respectively), compounds 5b, 5e (6) showed the most potent anticancer activity against DU-145 cell line (IC50 = 36.1 µM, 44.3 µM respectively) and compounds 3a (6) and 5g showed the most potent anticancer activity against LNCaP cell line (IC50 = 92.8 µM, 73.7 µM respectively). In this study, we also investigated molecular modeling of compounds on methionine aminopeptidase (type II) enzyme active site in order to get insight into binding mode and energy.

CONCLUSIONS:

The new naproxen derivatives [3,5a-h] were proven by FT-IR, 1H-NMR and elemental analysis data, which were evaluated for anticancer effect against PC-3, DU-145 and LNCaP cell lines. We observed best anticancer activity against PC-3 and DU-145 cell lines.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (Project number: 215S009).

REFERENCES:

1. Motawi TM. et. al. (2014). J Enzyme Inhib Med Chem, 29(2):153-161.
2. Küçükgüzel ŞG, Coşkun GP, (2016). Anticancer Agents Med Chem,16(10)
3. Küçükgüzel ŞG, Süzgün PÇ, (2015). Eur. J. Med. Chem., 97:830-870.
4. Çoruh I, et. al. (2018). Arch Pharm (Weinheim). Apr;351(3-4)
5. Amir M, et. al. (2007). Arch. Pharm. Chem. Life Sci. 340: 577-585.
6. Birgül K, et. al. (2017) VII EFMC International Symposium on Advances in Synthetic and Medicinal Chemistry, Vienna Austria.

P-458: IN SILICO STUDIES OF SOME 2-AMINO BENZOTHIAZOLE DERIVATIVES AS ALDOSE REDUCTASE ENZYME INHIBITORS

Bolelli, K., Ertan Bolelli, T., Yalcin, I.

Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

INTRODUCTION:

Diabetes Mellitus is a metabolic disease affecting around millions of people worldwide and it is anticipated a 85 % increase by the year 2025 (1). In diabetic condition, polyol pathway contributes for metabolism of 30% sugar as compared to 3% in normal condition. Aldose reductase enzyme is crucial due to polyol pathway involved in conversion of glucose into sorbitol (2).

MATERIALS AND METHODS:

In this study, in order to gain new insight concerns the possible binding modes of aldose reductase inhibitors. Docking studies of some 2-amino benzothiazole derivatives (3) were carried out by using Biovia Discovery Studio 3.5 software (4).

RESULTS:

Known inhibitor, Zopolrestat (ZST), and our compounds were docked into the aldose reductase enzyme. Docking results demonstrated that our compounds are bound to the enzyme active site and some of the compounds showed interactions with some aminoacids which is similar to the X-ray structure of the protein and ZST.

CONCLUSIONS:

According to the docking results, it can be considered that this results can lead the way for development of new aldose reductase inhibitors.

REFERENCES:

1. Wild S, Roglic G, Green A, Sicree R, King H (2004). Diabetes Care, 27:1047–1053.
2. Kinoshita JH, Nishimura C (1988). Diabetes Metab. Res. Rev., 4:323–337.
3. Bolelli K, Musdal Y, Aki Yalcin E, Mannervik B, Yalcin I (2017). SAR QSAR Environ. Res., 28:927-940.
4. Dassault Systèmes BIOVIA, Discovery Studio 3.5, San Diego: Dassault Systèmes, 2012.

P-459: SYNTHESIS AND EVALUATION OF ANTIOXIDANT ACTIVITY OF MELATONIN ANALOGUE NEW INDOLE DERIVATIVES

[1] Durgun, K., [1] Karaaslan, C., [2] Ince, E., [2] Gurer Orhan, H., [1] Suzen, S

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

[2]Ege University, Faculty of Pharmacy, Department of Toxicology, Izmir, Turkey

INTRODUCTION:

Reactive oxygen species (ROS) and reactive nitrogen species (RNS) are generated in different parts of the body and has toxic effects on macromolecules like lipids, proteins and even DNA. Antioxidant molecules can scavenge free radicals and prevent the damage on the vital molecules. Therefore a balance between antioxidants and the free radicals is necessary (1). Melatonin and some of its metabolites behaves as an antioxidant by scavenging free radicals and increasing the activity of antioxidant enzymes existing in body (2). The aim of this study was to synthesize and examine possible in vitro antioxidant effects of indole-based melatonin analog compounds.

MATERIALS AND METHODS:

As a part of our ongoing study nineteen indole hydrazide/hydrazone derivatives were synthesized, characterized and their in-vitro antioxidant activity was investigated by measurement of ROS with DCFH and DPPH methods. Cytotoxicity study of the synthesized compounds were established by MTT method.

RESULTS:

According to the studies, none of the products possessed vital decrease in cell viability so they don't have the potential of cytotoxicity. Also, we have observed antioxidant activity for all the synthesized compounds. Three compounds with methyl group substituted on the phenyl ring have shown less antioxidant activity than the others. For the DCFH method, the compounds haven't shown radical scavenging activity.

CONCLUSION:

Antioxidants can prevent the damage free radicals cause on macromolecules and tissues. These results have found promising for further research on antioxidant activity studies of indole-based melatonin analogs.

REFERENCES:

1. Lobo V, Patil A et al., (2010). Pharmacognosy Reviews, 4(8):118-126.
2. Gurer Orhan H, Suzen S (2015). Current Medicinal Chemistry, 22(4):490-498.

P-460: SYNTHESIS, IN VITRO AND IN SILICO STUDIES OF A SERIES OF 1,3,4-OXADIAZOLES AS FAK INHIBITORS.

[1] Altintop, MD., [1] Sever, B., [1] Ozdemir, A., [2] Akalin Ciftci, G

[1] Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskişehir, Turkey

[2] Anadolu University, Faculty of Pharmacy, Department of Biochemistry, Eskişehir, Turkey

INTRODUCTION:

Focal adhesion kinase (FAK) is a non-receptor cytoplasmic tyrosine kinase that is activated and/or overexpressed in a variety of human cancers. FAK promotes tumor progression and metastasis through effects on both tumor cells and stromal cells (1). As a result, inhibition of FAK has been recognized as an attractive therapeutic approach in oncology. Due to the significance of 1,3,4-oxadiazoles as potential FAK inhibitors (2), we aimed to design and synthesize new oxadiazole-based FAK inhibitors.

MATERIALS AND METHODS:

New oxadiazole derivatives (1-9) were synthesized via the reaction of 5-[((5,6,7,8-tetrahydronaphthalen-2-yl)oxy)methyl]-1,3,4-oxadiazole-2(3H)-thione with 2-chloro-N-(thiazol/benzothiazol-2-yl)acetamides. The inhibitory effects of the compounds on FAK (Phospho-Tyr397) activity in C6 rat glioma cell line were determined using Colorimetric Cell-Based ELISA FAK (Phospho-Tyr397) activity kit. Molecular docking studies were also performed to provide reasonable explanations for the most effective inhibitor in the active site of FAK (PDB code: 5TO8) (3) using Schrödinger's Maestro molecular modeling package.

Results: *N*-(6-Fluorobenzothiazol-2-yl)-2-[[5-[((5,6,7,8-tetrahydronaphthalen-2-yl)oxy)methyl]-1,3,4-oxadiazol-2-yl]thio]acetamide (**2**) showed significant FAK inhibitory activity (46.56±2.65%) in C6 cell line. This outcome indicated that the fluoro substituent at the 6th position of the benzothiazole ring enhanced FAK inhibitory activity. According to molecular docking studies, 6-fluorobenzothiazole ring of compound **2** displayed π-π interaction with Phe568 residue. Moreover, acetamido moiety of compound **2** presented H-bond and salt bridge formation with the in pocket residue Lys457 of the binding site of FAK.

CONCLUSIONS:

According to the in vitro and in silico studies, compound 2 stands out as a promising candidate for further studies.

REFERENCES:

1. Roy Luzarraga M, Hodivala Dilke K (2016). Clinical Cancer Research, 22(15):3718-3724.
2. Bajaj S, Asati V, Singh J, Roy PP (2015). European Journal of Medicinal Chemistry, 97:124–141.
3. Farand J, Mai N, Chandrasekhar J et al., (2016). Bioorganic & Medicinal Chemistry Letters, 26: 5926-5930.

P-461: SYNTHESIS OF SOME NOVEL N-SUBSTITUTED 4-(1H-BENZIMIDAZOL-1-YL)-BENZAMIDE DERIVATIVES

Alp, M.

Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

INTRODUCTION:

In our previous papers, we have reported the synthesis of benzimidazole derivatives and their promising anticancer activity results (1,2). These results promted us to synthesis and evaluation of some novel N-Substituted 4-(1H-benzimidazol-1-yl)-benzamide derivatives.

MATERIALS AND METHODS:

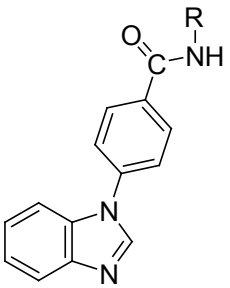
The 1H-benzimidazole ring was built by cyclization of the o-phenylenediamine and formic acid (3). And then reaction of the 1H-benzimidazole with ethyl 4-fluorobenzoate in DMF in the presence of anhydrous K2CO3 gave ethyl 4-(1H-benzimidazol-1-yl)benzoate. The acid derivative was obtained by hydrolyzing the ethyl ester in 5% NaOH (4). A solution of 4-(1H-benzimidazol-1-yl)benzoic acide in DMF is treated with substituted amines, 1-ethyl-3(3- dimethylaminopropyl)carbodiimide and N-hydroxybenzotriazole, stirred at stirred at 80 0C for 12 hours and concentrated in vacuo. Purification of this resultant residue oil by column chromatography provides the corresponding benzimidazoles (Scheme 1).

RESULTS:

1H-NMR and 13C-NMR spectra were recorded employing a Varian Mercury 400 MHz FT-NMR spectrometer. Mass spectra were taken on a Waters Micromass ZQ connected with a Waters Alliance HPLC, using the ESI(+) method, with a C-18. Elemental analyses were performed using a Leco CHNS-932. All instrumental analysis results of the synthesized compounds were found to be consistent with their chemical structures.

CONCLUSIONS:

Anticancer activity studies of these compounds are in progress.



Scheme 1. General formula of novel benzimidazole derivatives

REFERENCES:

1. Alp M, Goker H, Ozkan T, et al., (2014) Archives of Pharmacal Research, 37: 580-587.
2. Alp M, Gurkan Alp AS, et al., (2015) Zeitschrift für Naturforschung C, 70:79-85.
3. Furniss BS, Hannaford AJ, et al., (1989) Vogel's Textbook of Practical Organic Chemistry, Longman Scientific and Technical, UK, pp 1162-1163.
4. Aijaz, A, Lama P et al., (2010) New J. Chem., 34: 2502-2514.

P-462: STUDIES ON THE SYNTHESIS AND ALDOSE REDUCTASE ENZYME INHIBITION PROPERTIES OF NOVEL THIAZOLE DERIVATIVES

[1] Ceylan Unlusoy, M., [2] Sarikaya, M., [2] Das Evcimen, N., [1] Bozdag Dundar, O.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

[2]Ankara University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey

INTRODUCTION:

The Aldose reductase (AR) is the first enzyme of the polyol pathway. At normal physiological glucose concentrations, the majority of metabolic flux is directed through the glycolic pathway. However, under the hyperglycemic conditions frequently found in diabetics, a significant portion is directed through the polyol pathway where AR is responsible for the NADPH-dependent reduction of glucose to sorbitol (1). The acceleration of the polyol pathway thus elicits various metabolic imbalances in those tissues that undergo insulin-independent uptake of glucose. Such metabolic perturbation provokes the early tissue damage in the "target" organs of diabetic complications, such as ocular lens, retina, peripheral nerve, and renal glomerulus (2). Currently, epalrestat is the only Aldose reductase inhibitor (ARI) available for the therapy (3). Despite the difficulties in developing effective ARIs, the inhibition of AR has continued to be considered an attractive route to prevent or manage diabetic complications. As a part of our ongoing study a new series of 2-(pyrrolidin-1-yl)/ morpholino thiazolyl-2,4-thiazolidinedione / rhodanine compounds was synthesized and tested for their AR inhibition activities.

MATERIALS AND METHODS:

All compounds were synthesized via Knoevenagel Condensation reaction of substituted thiazole and TZD/rhodanine rings. Thiazolidinedione ester compounds were hydrolyzed for obtaining the acidic compounds. Their structure was characterized by 1H NMR, Mass and elementary analysis data. All compounds were tested for their in vitro aldose reductase inhibitory activities. Aldose reductase enzyme is isolated from rat lenses and the activity of the enzyme is determined by spectrophotometric method.

RESULTS:

All 1H NMR, Mass and elementary analysis data were in accordance with assumed structures**.** It was found that rhodanine acetic acid derivatives have significant inhibitor activities with the 83.39-91.94% inhibition.

CONCLUSIONS:

Among the synthesized compounds, rhodanine acetic acid moiety is found to be important for the ARI activity. These compounds can be the key formula of future studies.

ACKNOWLEDGEMENTS:

This study was supported by Research Organization of Ankara University, Turkey (No: 2005-0803048)

REFERENCES

1. Lori I, Robins SM, Dixon D et al., (2006). Bioorg. Med. Chem. 14:7728-7735.
2. Yabe-Nishimura C (1998). Pharmacol. Rev. 50(1):21-33.
3. Qin X, Hao X, Han H, et al., (2015). J. Med. Chem. 58:1254-1267.

P-463: STUDIES ON SOME BENZOTHIAZOLE DERIVATIVES

[1] Zengin, M., [1] Balkan, A., [1] Tan Unsal, O., [2] Kucukkilinc Tuylu, T., [2] Ayazgok, B.

[1] Hacettepe University, Department of Pharmaceutical Chemistry, Ankara, Turkey

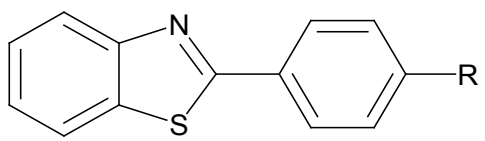
[2] Hacettepe University, Department of Biochemistry, Ankara, Turkey

INTRODUCTION:

Alzheimer Disease (AD) having a devastating effect on people is a mortally progressing neurodegenerative disorder (1). On the neuropathology of AD, amyloid plaques consisting of β-amyloid (Aβ) aggregation and storing, play an important role. Pursuant to this hypothesis some of the aims of new drug development activities are to reduce the Aβ formation, hinder the aggregation and increase the fragmentation (2). According to various studies some compounds carrying benzothiazole structure have shown inhibitory effect on the formation of Aβ fibrils which are playing a role at AD (3). The aim of this study is to clarify the structure of some new benzo[d]thiazole derivatives carrying 4-substitutedphenyl structure and to evaluate their Aβ fibril inhibitory activities.

MATERIALS AND METHODS:

The starting compounds, 4-substitutebenzaldehydes were obtained by treating 4-fluorobenzaldehyde with appropriate amines. The target compounds, 2-(4-substitutedphenyl)benzo[d]thiazoles (Fig.) were gained by the reaction of 4- substitutedbenzaldehydes with 2-aminothiophenol. The compounds were tested for their ability to inhibit self-mediated Aβ aggregation using the thioflavin T (ThT) fluorescence assay. Rifampicin and donepezil were used as reference compounds.



R: Azoles, 4-substitutedpiperazines

Fig.: General structure of 2-(4-substitutedphenyl) benzo[d]thiazole derivatives

RESULTS:

In this study, a series of 2-(4-substitutedphenyl) benzo[d]thiazole were synthesized. Structures of the synthesized compounds were elucidated by using spectral methods (IR, 1H-NMR, 13C-NMR, ESI-MS) and elemental analysis. Among the synthesized compounds, the derivatives carrying azole moities (imidazole, triazole and benzimidazole) showed more potent activity on Aβ aggregation than donepezil and rifampicin.

CONCLUSIONS:

All these results suggested that 2-phenylbenzo[d] thiazole with azole moities could be promising lead candidates against AD.

ACKNOWLEDGEMENTS:

This study was supported by Hacettepe University Scientific Research Coordination Unit (Project no: THD-2018- 16569)

REFERENCES:

1. Pejchal V., et. al., (2016). Bioorg. Med. Chem., 24:1560-1572.
2. Imramovsky A., et. al., (2013). Bioorg. Med. Chem., 21:1735-1748.
3. Gan CS., et al., (2013). Med. Chem. Res., 22:4069-4074.

P-464: STUDIES ON ANTIMICROBIAL PROPERTIES OF SOME BENZIMIDAZOLES

[1] Erol, M., [2] Temiz Arpaci, O., [2] Goker, H., [3] Kaynak Onurdag, F., and [3] Okten, S.

1 Erciyes University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Kayseri, Turkey

2Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey.

3 Trakya University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Edirne, Turkey

INTRODUCTION:

The usage of most antimicrobial agents is limited, not only by the rapidly developing drug resistance, but also by the unsatisfactory status of present treatments of microbial infectious and by drug side effects (1). Benzimidazole compounds are important fragments in medicinal chemistry because of their wide range of biological activities including antimicrobial activity (2).

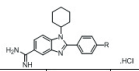
MATERIALS AND METHODS:

The benzimidazoles (compounds 2-8) were evaluated for their antimicrobial activity with microdilution technique described by CLSI. (3-4).

RESULTS:

The minimum inhibitory concentrations (MIC) of the new some benzimidazoles, were determined against standard bacterial and fungal strains and drug-resistant isolates and compared to those of several reference drugs and all the observed in vitro antimicrobial activity results of the tested compounds are given Table 1.

Table 1. Antimicrobial activity results (MIC µg/ml) of the compounds with the standard drugs



Comp. no.	-R	*E.coli* ATCC 25922	*E.coli* isolate	*P. aeruginosa* ATCC 27853	*P. aeruginosa* isolate	*S.aureus* ATCC 29213	MRSA	*E. faecalis* ATCC 29212	VRE	*C. albicans* ATCC 10231
2	-Cl	128	128	64	512	512	512	512	512	512
3	-Br	128	128	64	64	8	8	16	16	16
4	$-CH_3$	128	128	128	128	16	32	64	64	64
5	$-C_2H_5$	128	128	128	128	8	16	32	32	32
6	$-OCH_3$	32	32	128	128	8	16	32	32	128
7	-COOH	128	256	64	64	128	256	128	128	128
8	-benzyloxi	128	128	64	64	8	8	8	8	8
9	-dimethylamine	64	64	64	64	32	64	32	64	128

CONCLUSIONS:

In this study, we aimed to develop new effective antimicrobial agents possessing benzimidazole nuclei in their structure. Microbiological results showed that new benzimidazole derivatives possess an antimicrobial activity having MIC values of 8-512 µg/ml against the tested microorganisms.

ACKNOWLEDGEMENTS:

This work was supported by the TUBİTAK (Grant No. 315S333).

REFERENCES

1. Mohammed AM, Magdy MG, Magde NN, Waleed AHB (2004). Arch. Pharm. Med. Chem. 337: 427.
2. Mahalakshmi CM, Chidambaranathan V (2015). Int. J. Chem. Sci., 205–212
3. Clinical and Laboratory Laboratory Standards Institute (CLSI) (formerly NCCLS) Performance Standards for Antimicrobial Susceptibility Testing; 16th Informational Supplement. CLSI M100-S18. Clinical and Laboratory Standards Institute, 940 West Valley Road, Wayne, Pennsylvania, USA, 2008.
4. Clinical and Laboratory Standards Institute (CLSI) (formerly NCCLS): Reference method for broth dilution antifungal susceptibility testing yeast, approved standard, M27-A3. Clinical and Laboratory Standards Institute, 940 West Valley Road, Wayne, Pennsylvania, USA, 2006.

P-465: SYNTHESIS AND STRUCTURE ELUCIDATION OF SOME NOVEL BENZOXAZOLE DERIVATES

[1] Erol, M., [2] Temiz Arpaci, O.

[1] Erciyes University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Kayseri, Turkey

[2] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey.

INTRODUCTION:

Benzoxazoles are structural isosteres of natural nucleotides that can interact with biopolymers, constitute an important class of heterocyclic compounds. So that benzoxazoles showed several activities like antitumor, antiviral and antimicrobial activities (1-4).

MATERIALS AND METHODS:

Melting points were determined on a Buchi B-540 melting point apparatus in open capillary tubes and are uncorrected. Elemental analyses were done a Leco CHNS 932 elemental analyzer. 1H-NMR and 13C-NMR spectra were recorded on a Varian Mercury 400 MHz spectrometer using DMSO-d6. Mass spectra were acquired on a Waters Micromass ZQ using the ESI(+) method.

RESULTS:

In this study, firstly, 5-Amino-2-(p-tert-butylphenyl)-benzoxazole (1) was synthesized by heating 2,4-diaminophenol with p-tert-butyl benzoic acid in PPA. Then compound 2 was obtained by treating a solution of 3-choloropropionylchloride with 5-amino-2-(p-tert-butyl phenyl)-benzoxazole. To obtaine result compounds (3-12) (Figure), finally, compound 2 was treated by some morpholine, 4-(p-substituted piperazine/piperidine derivatives.

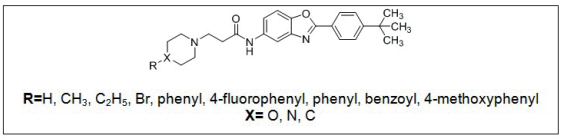


Figure. Synthesized compounds

CONCLUSIONS:

All the results compounds (compound 3-12) were prepared as original products. The structures of them were supported by spectral data. The 1H-NMR, 13C NMR, mass spectra and elemental analysis results agree with those of the proposed structures.

REFERENCES

1. Temiz Arpaci O, Cifcioglu Goztepe BE, Kaynak Onurdag F, Ozgen S, Senol FS, Erdogan Orhan I (2013). Acta Biol. Hung, 64:249-261.
2. Arisoy M, Temiz-Arpaci O, Kaynak-Onurdag F, Ozgen S (2012). Z. Naturforsch, 67c:466-472.
3. Akbay A, Oren I, Temiz-Arpaci O, Aki-Sener E, Yalcin I (2003). Arzneim Forsch, 53(4):266-271.
4. Pinar A, Yurdakul P, Yildiz I, Temiz Arpaci O, Acan NL, Aki Sener E, Yalcin I (2004). Biochem. Biophy. Res. Comm., 317:670-674.

P-466: SYNTHESIS AND ANTITUBERCULAR ACTIVITY EVALUATION OF 4-NAPHTHYL-1,4-DIHYDROPYRIDINE DERIVATIVES

[1] Gunduz, MG., [2] Krishna, VS., [2] Sriram, D.,[3] Weiss, N., [1] Simsek, R., [1] Safak, C.

[1] Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

[2] Birla Institute of Technology & Science-Pilani, Department of Pharmacy, Hyderabad campus, Jawahar nagar, Hyderabad, India

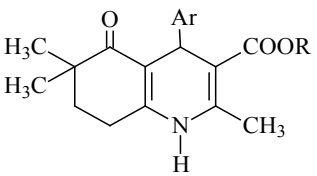
[3] Czech Academy of Sciences, Institute of Organic Chemistry and Biochemistry, Prague, Czech Republic

INTRODUCTION:

Tuberculosis (TB) is one of the most important infectious diseases caused by Mycobacterium tuberculosis and still remains a major global health problem (1). 1,4-Dihydropyridines (1,4-DHPs) block L-type calcium channel and therefore are used to treat hypertension. While designing 1,4-DHPs as antitubercular agents, calcium channel blocking activity can be one of the most important side effects (2). In this study, we aimed to present sixteen condensed 1,4-dihydropyridine derivatives with reduced calcium channel blocking effects as antimycobacterial agents.

MATERIALS AND METHODS:

Target compounds were achieved using modified Hantzsch reaction under microwave irradiation. In vitro anti-tubercular activity of the compounds was evaluated against *Mycobacterium tuberculosis* H37Rv. Their effects on L-type calcium channel were tested using patch clamp assay.



Ar: 1-Naphthyl, 2-Naphthyl
R: CH_3, C_2H_5, $CH(CH_3)_2$, $CH_2CH(CH_3)_2$, $C(CH_3)_3$, $CH_2CH_2OCH_3$, $CH_2CH_2OCOC(=CH_2)CH_3$, $CH_2C_6H_5$

RESULTS:

The obtained results indicated that some compounds bearing liphophilic ester groups exhibited very good antimycobacterial activity (MIC: 0.78-1.56 µg/ml). Introducing naphthl ring as an aromatic substituent at 4-position of the 1,4-DHP ring lead to a decrease in calcium channel blocking activity compared to phenyl ring.

CONCLUSIONS:

In this study, antitubercular activities of sixteen condensed 1,4-DHP (hexahydroquinoline) derivatives were reported. Four compounds, which were found to be very active, were also tested for their calcium channel blocking activity. Our data suggest that a condensed dihydropyridine-based scaffold with the naphthyl ring may serve as a new pharmacophore for antimycobacterial activity with reduced calcium channel blocking effects.

REFERENCES:

1. Palomino JC, Martin A (2013.) Journal of Antimicrobial Chemotherapy, 68:275-283.
2. Trivedi AR, Dodiya DK, Dholariya BH, Kataria VB, Bhuva VR, Shah VH (2011). Bioorganic&Medicinal Chemistry Letters, 21:5181-5183.

P-467: SYNTHESIS AND ANTICANCER ACTIVITY OF 4-HYDROXY BENZOIC ACID HYDRAZIDE-HYDRAZONES

[1] Han, MI., [1] Cagan, B., [2] Dinparvar, S., [2] Allahverdiyev, A., [1] Kucukguzel, SG.

[1]Marmara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, İstanbul, Turkey

[2]Yıldız Teknik University, Faculty of Chemistry-Metallurgical, Department of Bioengineering, İstanbul, Turkey

INTRODUCTION:

Hydrazide-hydrazones have been reported various pharmacological activities (1-6). Ethyl paraben, ethyl-4-hydroxybenzoate, is a protective compound which has used for stability effects in drugs, foods or cosmetic preparates. Ethyl paraben was chosen as a starting substance to synthesize new hydrazide-hydrazones.

MATERIALS AND METHODS:

Ethyl-4-hydroxybenzoate was used as the starting compound to design several novel hydrazide-hydrazones. The reaction of ethyl-4-hydroxybenzoate with hydrazine-hydrate in ethanol resulted in 4-hydroxybenzoic acid hydrazide. 4-Hydroxybenzoic acid hydrazide was condensed with substituted aromatic aldehydes in ethanolic medium with refluxed to obtain new hydrazide-hydrazones. The synthesized compounds evaluated anticancer activity against MCF-7 (breast adenocarcinoma) and AU565 (breast adenocarcinoma) cancer cell lines (7).

RESULTS:

The purity of synthesized compounds was controlled by thin layer chromotgraphy, elemental analysis, high pressure liquid chrotomography and melting points. Their structures were elucidated with FT-IR and 1H-NMR spectroscopy. FT-IR spectral data of novel hydrazide-hydrazones were observed hydrazone N-H, hydrazone C=O and C=N streching data between 3041-3072, 1687-1680, and 1606-1602 cm-1, respectively. The chemical shift of the azomethine proton and –NH-proton of acylhydrazone moiety in hydrazide-hydrazones were detected in the range of 8.45-8.71 ppm and 11.73-12.07 ppm, respectively.

CONCLUSIONS:

New 4-hydroxybenzoic acid hydrazide-hydrazones were synthesized, characterized and evaluated anticancer activity against breast adenocarcinoma cancer cell lines.

REFERENCES:

1. Rollas S, Kucukguzel SG (2007). Molecules, 12: 1910-1939.
2. Kucukguzel SG, Mazi A, Sahin F, Ozturk S, Stables J (2003). Eur J Med Chem, 38: 1005-1013.
3. Aydın S, Basu NK, Arora P, Basu A, Nichols DB, Talele TT, Akkurt M, Çelik İ, Büyükgüngör O, Kucukguzel SG (2013). Marmara Pharmaceutical Journal 17: 181-189.
4. Cikla P, Ozsavcı D, Ozakpinar OB, Sener A, Cevik O, Turan SO, Akbuga J, Sahin F, Kucukguzel SG (2013). Arch Pharm, 346(5): 367-379.
5. Kucukguzel SG, Koc D, Cikla P, Ozsavci D, Ozakpinar OB, Tiber PM, Orun O, Erzincan P, Erdem SS, Sahin F (2015). Arch Pharm, 348(10): 730-742.
6. Senkardes S, Basu NK, Durmaz I, Manvar D, Basu A, Atalay R, Kucukguzel SG (2016). Eur J Med Chem, 108: 301-308.
7. Abamor ES, Allahverdiyev AM (2016). Experimental Parasitology, 166: 150-163.

P-468: SYNTHESIS AND SCREENING FOR CYTOTOXIC EFFECTS OF KOJIC ACID DERIVATIVES ON A375 HUMAN MALIGNANT MELANOMA

[1] Aytemir, MD., [1] Karakaya, G., [2] Ercan, A., [2] Oncul, S.

[1]Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey.

[2]Hacettepe University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey.

INTRODUCTION:

Malignant melanoma is one of the most serious type of skin cancers with increasing prevalence and mortality rates. Although it constitutes only 4% of the skin cancers, melanoma accounts for 75% of skin cancer-related deaths. Numerous agents are currently under development to provide alternative therapeutic options (1). Previously, a large number of Mannich bases using kojic acid (5-hydroxy-2-(hydroxymethyl)-4H-pyran-4-one) as the starting material were synthesized and examined in our laboratory for their various types of biological actions including anticonvulsant, antiviral, anti-bacterial, anti-fungal, anti-mycobacterial, anti-oxidant, anti-aging and anti-tyrosinase activities besides cytotoxic effects (2-4).

MATERIALS AND METHODS:

Chlorination of the 2-hydroxymethyl moiety of kojic acid using thionyl chloride at room temperature produced chlorokojic acid (2-chloromethyl-5-hydroxy-4H-pyran-4-one), with the ring hydroxyl being unaffected. Allomaltol (5-hydroxy-2-methyl-4H-pyran-4-one) was obtained by the reduction of chlorokojic acid with zinc dust in hydrochloric acid. Mannich bases with the structure of 2-substituted-3-hydroxy-6-hyroxymethyl/chloromethyl/ methyl/4H-pyran-4-one (compounds 1-14) were synthesized by the reaction of kojic acid/chlorokojic acid/allomaltol and substituted benzylpiperazine derivatives in presence of formaline at room temperature. Viability of A375 human malignant melanoma cell exposed to the compound was assessed by sulforhodamine B (SRB) assay. SRB assay is a colorimetric method based on measurement of cellular protein content and used for the determination of cytotoxicity (5). Vemurafenib, dacarbazine, temozolomide, lenalidomide and fotemustine currently used in the treatment of malign melanoma were utilized as control agents.

RESULTS:

New eleven Mannich bases having structure of 2-substituted-3-hydroxy-6-hydroxymethyl/chloromethyl/methyl/-4H-pyran-4-one were synthesized with quite significant yield. The structures of the compounds were identified by using techniques IR, 1H-NMR, 13C-NMR, mass spectroscopy and elementary analysis. None of the compounds 1-14 showed activity as much as vemurafenib (IC50: 4.6 μM) and dacarbazine (IC50: 69.6 μM). It was found that the cytotoxicity effect of the compounds 1-14 (IC50: 73.74-95.59 μM) were higher than temozolomide (IC50: 95.6 μM) and lenalidomide (IC50: 143.1 μM).

CONCLUSIONS:

This study suggests that in the future together with in vivo applications, these compounds can be used as a promising research model on the treatment of malignant melanoma.

ACKNOWLEDGEMENTS:

This research was funded as a project by TÜBİTAK (SBAG-315S067) and Hacettepe University Scientific Research Fond (THD-2015-7392).

REFERENCES:

1. Chang, TW, Weaver AL, Brewer JD, Kyle RA, Baum CL (2017). Journal of the American Academy of Dermatology, 78(3):621-371.
2. Aytemir MD, Ozcelik B (2010). European Journal of Medicinal Chemistry, 45(9):4089-95.
3. Karakaya G, Aytemir MD, Ozcelik B, Calis, Ü (2013). Journal of Enzyme Inhibition and Medicinal Chemistry, 28(3):627-38.
4. Aytemir M, Ozcelik B, Orhan IE, Karakaya G Senol FS (2015) Biological effect of Mannich bases of kojic acid derivatives. Turkish Patent TR 2015 07653 B.
5. Vichai V, Kirtikara K (2006). Natural Protocol, 1:1112-6.

P-469: DOCKING STUDIES OF KOJYLMETHYL DICHLOROBENZYL PIPERAZINE AS A TYROSINASE INHIBITOR

[1] Aytemir, MD., [2] Demirci, A., [1] Karakaya, G.

[1]Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey.

[2]Marmara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Istanbul, Turkey.

INTRODUCTION:

Tyrosinase is a key regulatory enzyme responsible for melanin production in melanocytes and widely distributed in nature. Since tyrosinase plays a critical role in melanin production, inhibitors of tyrosinase enzyme have become increasingly important in medicinal chemistry for developing new depigmenting agents used in pharmacological and cosmetic fields. Among the many kinds of tyrosinase inhibitors, kojic acid (5-hydroxy-2-hydroxymethyl-4H-pyran-4-one) is commonly used and well known with its antityrosinase property (1). In our previous study, Mannich bases of kojic acid (5-hydroxy-2-(hydroxymethyl)-4H-pyran-4-one) including 3,4-dichlorobenzylpiperazine substituent (KOJI MG84; 3-hydroxy-6-(hydroxymethyl)-2-[[4-(3,4-dichlorobenzyl)piperazine-1-yl]methyl]-4H-pyran-4-one) and 2,6-dichlorobenzyl- piperazine substituent were synthesized by the reaction of kojic acid with substituted benzylpiperazine derivatives in the presence of formaline without by-product formation at room temperature. Their anti-tyrosinase, anti-aging, anti-mycobacterial, anti-dermatofitic and anti-oxidant activities were evaluated. The results were reported and patented with the title of “Kojic Acid-Derived Mannich Bases with Biological Effect” (2). The potential inhibitory activity of KOJI MG84 was investigated in silico using molecular docking simulation method (3).

MATERIALS AND METHODS:

Agaricus bisporus tyrosinase enzyme (PDB ID: 2X9Y) was derived from Protein Data Bank. MGLTools and Biovia Discovery Studio Visualizer software were used to prepare data before docking. Holmium atom was removed from the structure and polar hydrogen atoms were added to protein for docking calculations. 3D structures of ligands were also prepared. Gasteiger charges were assigned to the ligands and the receptor. Protonation states of histidine amino acid residues were determined. Histidines apart from His61, His85, His94, His259, His263 and His296 were prepared as charged forms while mentioned histidine residues which bind to copper ions were assigned as 0HD1 forms. Autodock Vina software was used for docking calculations. Binding modes of the ligands were evaluated with PMV and PyMOL.

RESULTS:

We suggest a tyrosinase inhibition mechanism of Mannich bases through this study. Possible H-bond and hydrophobic interactions between the side chain of Mannich bases and tyrosinase enzyme active site are visualized with molecular modeling studies. According to the predicted conformation of KOJI MG84 in the A. bisporus tyrosinase enzyme binding site, hydroxymethyl group provides a metal complex with copper ions and enzyme. His61, His85, His94, His259, His263 and His296 residues prominently support this complex. Chlorine substitution to phenyl ring makes a weak hydrogen bond with Asn81. The 4th position oxygen atom of pyranone ring makes hydrogen bond interaction with Ser282.

CONCLUSIONS:

These in silico results can thus serve as a template for further in vitro and in vivo studies.

REFERENCES:

1. Noh JM, Kwak SY, Seo HS, SEo JH, Kim BG, Lee YS (2009). Bioorganic & Medicinal Chemistry Letters, 19:5586-89.
2. Aytemir M, Ozcelik B, Orhan IE, Karakaya G Senol FS (2015). Biological effect of Mannich bases of kojic acid derivatives. Turkish Patent TR 2015 07653 B.
3. Lai X, Wichers HJ, Soler-Lopez M, Dijkstra BW (2017). Angewandte Chemie International Edition in English, 56(33):9812-15.

P-470: SYNTHESIS, IN VITRO AND IN SILICO STUDIES OF A SERIES OF DITHIOCARBAMATE DERIVATIVES AS ANTICANDIDAL AGENTS.

Ozdemir, A., Yilmaz, N.,Sever, B., Altintop, MD.

Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskisehir, Turkey

INTRODUCTION:

Current antifungal therapy is limited by the short arsenal of antifungal agents, toxicity problems and the development of resistance (1). Due to the significance of dithiocarbamates in the field of antifungal drug design (2), we aimed to design and synthesize new dithiocarbamate-based anticandidal agents.

MATERIALS AND METHODS:

New dithiocarbamate derivatives (Fig. 1) were synthesized via the reaction of 1-(chloroacetyl)-3-(2-furyl)-5-(3,4-methylendioxyphenyl)-2-pyrazoline with sodium salts of N,N-disubstituted dithiocarbamic acids. These compounds were evaluated for their in vitro antifungal effects on Candida albicans, Candida glabrata, Candida parapsilosis and Candida krusei using a broth microdilution assay. Besides, molecular docking studies were carried out for the most effective

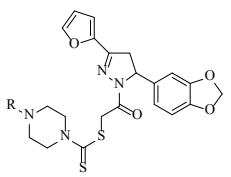
anticandidal agent in the active site of lanosterol 14α-demethylase enzyme CYP51 (PDB code: 5FSA) to provide any mechanistic insights into further in vitro enzyme studies (3).

RESULTS:

1-[((4-(4-Fluorophenyl)piperazin-1-yl) thiocarbamoylthio)acetyl]-3-(2-furyl)-5-(3,4-methylendioxyphenyl)-2-pyrazoline (2) was the most potent antifungal agent on C. parapsilosis with a MIC value of 15.63 µg/mL when compared with ketoconazole (MIC= 31.25 µg/mL). The fluoro substituent on the phenyl group at the 4th position of the piperazine ring enhanced antifungal activity against C. parapsilosis. According to molecular docking studies, compound 2 displayed π-π interaction with Tyr118 residue in the active site of CYP51. In silico studies suggest that 4-fluorophenyl moiety is crucial for the interactions with the binding area of the target structure.

CONCLUSIONS:

According to the in silico and in vitro studies, compound 2 stands out as a promising candidate for further in vitro studies.



Compound	R
1	Phenyl
2	4-Fluorophenyl
3	4-Methoxyphenyl
4	4-Nitrophenyl
5	2-Pyridiminyl
6	2-Hydroxyethyl
7	Ethyl
8	2-(Dimethylamino)ethyl
9	3-(Dimethylamino)propyl
10	Benzyl

Figure 1. The structures of compounds 1-10

REFERENCES:

1. Pierce CG, Lopez-Ribot JL (2013). Expert Opinion on Drug Discovery, 8(9):1117-1126.
2. Bala V, Gupta G, Sharma VL (2014). Mini-Reviews in Medicinal Chemistry, 14(12):1021-1032.
3. Schrödinger Release 2016-2: Schrödinger, LLC, New York, NY, USA.

P-471: DESIGN, SYNTHESIS, BIOLOGICAL EVALUATION AND MOLECULAR MODELING STUDIES OF NOVEL 5-ARYLIDENE-4-THIAZOLIDINONES AS SELECTIVE COX-2 INHIBITORS

[1] Kulabas, N., [2] Bingol Ozakpinar, O., [1] Kucukguzel, I.

[1] Marmara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Istanbul, Turkey

[2] Marmara University, Faculty of Pharmacy, Department of Biochemistry, Istanbul, Turkey

INTRODUCTION:

Cyclooxygenase-2 (COX-2)-selective inhibitors are safer anti-inflammatory agents with fewer gastrointestinal side effects than nonselective NSAIDs. In many studies, inhibition of COX-2 is proposed as a treatment option in several cancer types and neurological diseases [1]. 2-Imino-5-methylidene-1,3-thiazolidin-4-one derivatives are known to posses anti-inflammatory activity due to COX-2 inhibition, besides other biological effects (2-4).

MATERIALS AND METHODS:

In this study, sixteen 5-arylidene-2-[(4-chloropyridin-2-yl)imino]-1,3-thiazolidin-4-one derivatives were synthesized via Knoevenagel condensation of aromatic aldehydes with 2-[(4-chloropyridin-2-yl) imino]-1,3-thiazolidin-4-one, and identified by the help of IR, 1H-NMR, 13C-NMR and mass spectral data while their purities were proved by TLC and elemental analysis. The inhibitory potential of synthesized sixteen arylidene derivatives on COX-1 and COX-2 enzymes were evaluated using a “COX Inhibitor Screening Kit” at 10µM dose. The assay was conducted in duplicate and statistical analysis was carried out using GraphPad Prism 6.1 Software. The crystal structures of COX-1 (PDB code: 1Q4G) and COX-2 (PDB code: 3LN1) were used for docking after cleaning the enzyme structures from co-crystallized compounds and from water molecules. Three-dimentional structures of the synthesized compounds were optimized with semi-empirical PM3 method and used for initial geometry in docking calculations. The resultant docking files were analyzed to explain the mechanism of binding using Accelrys Discovery Studio Visualizer 4.0 program.

RESULTS:

The inhibitory effects on COX-1 and COX-2 enzymes of synthesized compounds were evaluated at 10 µM dose and were observed that 2-[(4-chloropyridin-2-yl)imino]-1,3-thiazolidin-4-one has lower than 50% inhibition value for both of enzymes while 5-arylidene derivatives exhibited selective COX inhibition by >70% COX-2 inhibition value. When interaction of synthesized compounds with the active site of the

COX enzymes were examined, it has been observed that 2-[(4-chloropyridin-2-yl)imino]-1,3-thiazolidin-4-one interacted with the active site of both enzymes. However 5-arylidene derivatives interacted only with the active site of COX-2 enzyme.

CONCLUSIONS:

These results showed that 5-arylidene substition of 2-imino-1,3-thiazolidinone derivatives enhances COX-2 selectivity. This study reveals important findings for the design of the new selective COX-2 inhibitors for further researchs.

ACKNOWLEDGEMENTS:

This study was supported by Scientific Research Project Commision of Marmara University (Project number: SAG-C-DRP-050614-0227). N.Kulabaş also thanks to the Scientific and Technological Research Council of Turkey (TUBITAK) for Domestic PhD Scholarship intended for Priority Areas (Code: 2211-C).

REFERENCES:

1. Dundar et al., (2009). Eur J Med Chem, 44:1830-1837.
2. Eleftheriou et al., (2012). Eur J Med Chem, 47:111-124.
3. Apostolidis et al., (2013). Bioorg Med Chem, 21: 532-539.
4. Song et al., (1999). J Med Chem, 42: 1151-1160.

P-472: SYNTHESIS AND ANTICANCER ACTIVITY OF NEW FLURBIPROFEN THIOETHERS AS METHIONINE AMINOPEPTIDASE (TYPE II) INHIBITORS

[1] Bayer, B., [2] Bekci, H., [3] Uba, AI., [2] Cumaoglu, A., [3] Yelekci K, [4] Yilmaz O., [1] Kucukguzel, SG.

[1]Marmara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, İstanbul, Turkey.

[2]Erciyes University, Faculty of Pharmacy, Department of Pharmaceutical Biochemistry, Kayseri, Turkey

[3]Kadir Has University, Faculty of Engineering and Natural Sciences, Department of Genetics and Bioengineering, İstanbul, Turkey

[4]TUBITAK Marmara Research Center, Kocaeli, Turkey

INTRODUCTION:

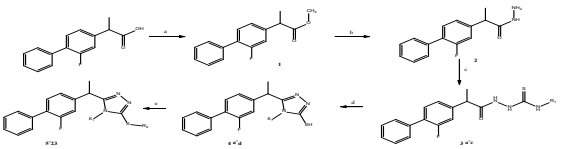
MetAP2 appears to play a critical role in cell proliferation and tumor growth. In recent years, containing of 1,2,4-triazoles moiety thioethers are reported as potential MetAP2 inhibitors (1).

MATERIALS AND METHODS:

Flurbiprofen, (R,S) 2-(2-fluoro-[1,1'-biphenyl]-4-il) propanoic acid, that have the structural skeleton of 2-arylpropionic acid was chosen as a starting substance to synthesize thioethers. Flurbiprofen was refluxed in the presence of methanol by catalyst saturated sulfuric acid to form methyl 2-(2-fluoro-[1,1'-biphenyl]-4-yl)propanoate (1). Methanolic solution of compound 1 and hydrazine hydrate were refluxed to obtain 2-(2-fluoro-[1,1'-biphenyl]-4-yl) propanehydrazide (2). Compound 2 and several isothiocyanates yield 2- (2- (2-fluoro- [1,1'-biphenyl] -4-yl) propanoyl) -N-alkyl /aryl thiosemicarbazides (3a-c). The thiosemicarbazides react with NaOH solutions (4N) and after cyclization reaction 3-(1-(2-fluoro[1,1'-biphenyl]-4-yl)ethyl)-4-substituted-1H-1,2,4-triazole-5(4H)-thiones(4a-d) are gained. To a suspension of 4-substituted-1,2,4-triazole-3-thione in ethanol containing anhydrous K2CO3, substituted benzyl chlorides was added to form the target compounds 3-(1-(2-fluoro-[1,1'-biphenyl]-4-yl)ethyl)-4-(substitutedphenyl/alkyl)-5-(substitutedsulfanyl)-4H-1,2,4-triazole (5-23).

RESULTS:

The structures of synthesized compounds were confirmed their structures by FT-IR, 1H-NMR and elemental analysis data, their impurty profiles were controlled by TLC. Among these compounds, compunds5 (2) and 21 showed the most potent anticancer activity against PC-3 cell line (IC50 = 27.1 µM , 5.12 µM, respectively), compounds 3c, 5 (2) and 23 showed the most potent anticancer activity against DU-145 cell line (IC50 = 11.55 µM , 6.9 µM , 9.54 µM, respectively), compounds 4d and 16showed the most potent anticancer activity against LnCAP cell line (IC50 = 11.45 µM , 26.91 µM, recpectively). In this study,we also investigated apoptotic mechanism and molecular modeling of compounds on methionine aminopeptidase (type II) enzyme active site in order to get insight into binding mode and energy.



(a) CH3OH / H2SO4; (b) NH2NH2.EtOH, (c) R1–NCS / EtOH; (d) NaOH (4N); (e) R2/ EtOH / K2CO3

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (Project number:215S009)

REFERENCES:

1. 1.Coruh I, Cevik O, Yelekci K, Djikic T, Kucukguzel SG. Arch Pharm(Weinheim). 2018 Mar doi: 10.1002/ardp.201700195, in press.
2. Yilmaz O, Bayer B, Han MI, Kucukguzel ŞG. 11th Asian Federation for Medicinal Chemistry's International Medicinal Chemistry Symposium, 23-26 Temmuz 2017, Melbourne Australia

P-473: ANTIMICROBIAL EVALUATION OF 2-METHYLINDOLE-HYDRAZONE DERIVATIVES

[1] Ozturk Ceylan, O., [1] Karaaslan, C., [2] Altanlar, N., [1] Suzen, S.

[1] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

[2] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Ankara, Turkey

INTRODUCTION:

The synthetically available and pharmacologically active indole scaffold has provided the incentive for the development of a number of antimicrobial compounds. Indoles and hydrazone-type molecules establish significant classes of pharmacologically active agents against especially multi-drug-resistant microbial infections. This presented research represent the anti-bacterial and anti-fungal activity results of 2-methylindole-3-carboxaldehyde hydrazone derivatives. (1)

MATERIALS AND METHODS:

These derivatives were tested for their in vitro antimicrobial activities using the two-fold serial dilution technique against Staphylococcus aureus, methicillin-resistant S. aureus, methicillin-resistant S. aureus isolate, Escherichia coli, Bacillus subtilis, and Candida albicans. The minimum inhibitory concentration (MIC) was determined for the test compounds and for the reference standards sultamicillin, ampicillin, fluconazole and ciprofloxacin. (2,3)

RESULTS:

All tested molecules showed a broad spectrum of activity having MIC values of 6.25–100 µg/ml against the tested microorganisms. Aromaticity and side chain as well as the halogens of the phenyl ring were found to be noteworthy for the antimicrobial activity

CONCLUSIONS:

The results may be instructive to researchers attempting to gain more understanding of the antimicrobial activity of indole hydrazide/hydrazone-type compounds. More research is needed to find effective indole-hydrazine type antimicrobial agent.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (109S099)

REFERENCES:

1. Lepri S, Buonerba F, Goracci L, Velilla I, Ruzziconi R, Schindler BD, Seo SM, Kaatz GW, Cruciani G (2016). J. Med. Chem., 59(3):867-891
2. Shirinzadeh H, Altanlar N, Yucel N, Ozden S, Suzen S (2011). Z Naturforsch C., 66(7-8):340-4.
3. Gurkok G, Altanlar N, Suzen S. (2009) Chemotherapy, 55(1):15-9.

P-474: ANTIMICROBIAL EVALUATION OF SOME HETEROCYCLIC COMPOUNDS

[1] Temiz Arpaci, O., [2] Erol, M., [3] Kaynak Onurdag, F. [3] Okten, S.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey.

[2] Erciyes University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Kayseri, Turkey

[3] Trakya University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Edirne, Turkey

INTRODUCTION:

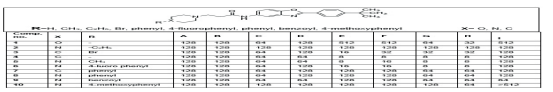
A benzoxazole derivative; calcimycin is a carboxylic polyether antibiotic from a strain of Streptomyces chartreusis (NRRL 3882). It was found to very active against gram-positive bacteria. So that benzoxazoles constitute an important class of heterocyclic compounds with antimicrobial and antibiotic activities [1-2].

MATERIALS AND METHODS:

The compounds were evaluated for their antimicrobial activity with microdilution technique described by CLSI. [4-5].

Results:The minimum inhibitory concentrations (MIC) of the new some benzoxazoles were determined against standard bacterial and fungal strains and drug-resistant isolates and compared to those of several reference drugs and all the observed in vitro antimicrobial activity results of the tested compounds are given Table 1.

Table 1. Antimicrobial activity results (MIC µg/ml) of new compounds with the standard drugs.



A: E. coli ATCC 25922, B: E. coli isolate, C: P.aeruginosa ATCC 27853, D: P. aeruginosa isolate, E: S.aureus ATCC 29213, F: MRSA, G: E.faecalis ATCC 29212, H: VRE, I: C.albicans ATCC 10231

CONCLUSIONS:

In this study, we aimed to develop new effective antimicrobial agents possessing benzoxazole ring as heterocyclic structure. Microbiological results showed that new heterocyclic compounds possess an antimicrobial activity having MIC values of 8-512 µg/ml against the tested microorganisms.

REFERENCES

1. Prudhomme M, Guyot J, Geminet G(1986). J. Antibiotics. 39: 934.
2. Arisoy M, Temiz Arpaci O, Kaynak Onurdag F, Ozgen S (2012). Z. Naturforsch. 67c:466-472.
3. Clinical and Laboratory Laboratory Standards Institute (CLSI) (formerly NCCLS): Performance Standards for Antimicrobial Susceptibility Testing; 16th Informational Supplement. CLSI M100-S18. Clinical and Laboratory Standards Institute, 940 West Valley Road, Wayne, Pennsylvania, USA, 2008.
4. Clinical and Laboratory Standards Institute (CLSI) (formerly NCCLS): Reference method for broth dilution antifungal susceptibility testing yeast, approved standard, M27-A3. Clinical and Laboratory Standards Institute, 940 West Valley Road, Wayne, Pennsylvania, USA, 2006.

P-475: SYNTHESIS OF SOME NOVEL AMIDINE DERIVATIVES

[1] Temiz Arpaci O., [2] Tasci, M., [1] Goker, H.

[1] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

[2] Erciyes University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Kayseri, Turkey

INTRODUCTION:

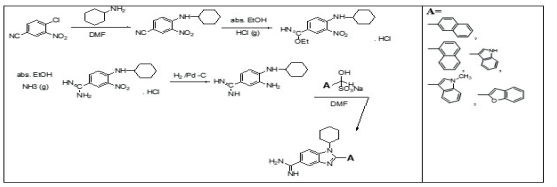
The aromatic amidines, such as berenil, pentamidine, propamidine and furamidine are well-known antimicrobial drugs also the antibiotic and anticancer activity of this kind of compounds has been described [1-2]. On the otherhand benzimidazole ring is structural isosteres of natural nucleotides and can interact with the biopolymers that they constitute an important class of heterocyclic compounds with antimicrobial and antifungal activity [3-4].

MATERIALS AND METHODS:

Melting points were determined on a Buchi B-540 melting point apparatus in open capillary tubes and are uncorrected. Elemental analyses were done a Leco CHNS 932 elemental analyzer. 1H-NMR and 13C-NMR spectra were recorded on a Varian Mercury 400 MHz spectrometer using DMSO-d6. Mass spectra were acquired on a Waters Micromass ZQ using the ESI(+) method.

RESULTS:

In the present investigation, a new series of amidine derivatives was synthesized using a multiple step procedure and the synthetic pathways for preparation of the target compounds are shown in Scheme.



Scheme. Synthesis of the target compounds

CONCLUSIONS:

In this study, we put some heterocyclic rings on second position and an amidine group on the fifth position of benzimidazole ring and synthesized them, the synthetic pathways for preparation of the target compounds are shown in Scheme. The structures of them were supported by spectral data. The 1H-NMR, 13C NMR and mass spectra and elemental analysis results agree with those of the proposed structures.

ACKNOWLEDGEMENTS:

This work was supported by the TUBITAK (Grant No. 315S333).

REFERENCES:

1. St-Germain G (1990). Antimicrob. Agents Chemother.,34:2304
2. Tao B, Huang TL, Zhang Q, Jackson L, Quener SF, Donkr IO (1999). Eur. J. Med. Chem., 34: 531.
3. Mahalakshmi CM, Chidambaranathan V (2015). Int. J. Chem. Sci., 13:205–212.
4. Goker H, Ozden S, Yildiz S, Boykin DW (2005). Europen Journal of Medicinal Chemistry, 40:1062-1069.

P-476: NOVEL 2-(PYRROLIDIN-1-YL) THIAZOLE DERIVATIVES AND THEIR ANTI(MYCO)BACTERIAL ACTIVITIES

[1] Belveren, S., [1] Poyraz, S., [2] Ulger, M., [1] Dondas, HA.

[1] Mersin University, Department of Analytical Chemistry, Mersin, Turkey

[2] Mersin University, Department of Pharmaceutical Microbiology, Mersin, Turkey

INTRODUCTION:

Heterocycles containining thiazole and/or pyrrolidine are useful building block for the construction of pharmaceutically important heterocycles and play important role in medicinal chemistry (1-3). In many report hybridization and modification of the heterocycles allow to obtain potential bioactive molecules and improve the pharmaceutical and biological activity comparing to starting lead compounds (4).Continuation of our ongoing research study (5), in this work we report the efficient preparation of such these new heterocycles, containining thiazole and/or pyrrolidine ring systems and determine their biological properties.

MATERIALS AND METHODS:

Azomethine ylide-1,3-dipolar cycloadditions cascade reaction applied to prepare highly functionalized polysubstituted pyrrolidine derivatives from corresponding iminoester and condensation reaction of pyrrolidine with aroyl isothiocyanate afforded desired aroylaminocarbo-N-thioylpyrrolidine intermediates. Further modification of these prepared compounds allowed to access novel highly functionalized hybrid heterocycles. Structures and stereochemistry of novel compounds were determined by NMR, MS, IR HRMS analytical techniques. Biological evaluation of these compounds were screened against antibacterial and anti-tuberculosis(TB) activity.

RESULTS:

The above mentioned process allowed us to obtain the desired novel potential bioactive hybrid compounds in good to excellent yields.The bioactivity of the tested compounds were found to be potential bioactive when screened against Staphylococcus aureus (ATCC 25925), Escherichia coli (ATCC 25923), Acinetobacter baumannii (ATCC 02026), Bacillus subtilis (ATCC 6633), Aeromonas hydrophila (ATCC 95080) and M. tuberculosis H37RV.

CONCLUSIONS:

The structural variation of the prepared hetereocycles depend on the nature of substituent at 2, 3 and 4-positions of the prolinates which originated from imines, dipolarophiles and its further modification.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Mersin University (Project no. BAP-SBE TEB(SB) 2017-2-TP3-2564).

REFERANCE

1. Dondas et al., (2017). Synthesis, 49: 2819–2851.
2. Varghese et al., (2016). World Journal of Pharmacy And Pharmaceutıcal Sciences, 5: 624-636.
3. Mąkosza M, Wojciechowski K (2015). Chemistry of Heterocyclic Compounds, Rew. 51: 210-222.
4. Bathini et al., (2017). European Journal of Medicinal Chemistry, 138: 83-95.
5. Belveren et al., (2017). Tetrahedron, 73: 6718-6727

P-477: COPPER(II) COMPLEXES OF N-BENZOYL-2-(1H-INDOL-2-YL) PYRROLIDINE-1-CARBOTHIOAMIDE AND THEIR BIOLOGICAL EVALUATION

[1] Poyraz, S., [1] Belveren, S., [2] Ulger, M., [1] Dondas, HA.

[1] Mersin University, Department of Analytical Chemistry, Mersin, Turkey

[2] Mersin University, Department of Pharmaceutical Microbiology, Mersin, Turkey

INTRODUCTION:

Current interest in the preparation and their biological evaluation for the Cu complexes is getting increase because of their potential use as bioactive agents such as antitumoral, antiviral and antimicrobial properties (1) and some Cu complexes were found to be potential non-steroidal anti-inflammatory drugs (2). Pyrrolidine and carbothioamide derivatives are important structural features owing to their pharmaceutical properties and can be utilised for the preparation of bioactive hetereocycles (3, 4). In this study, we focused on to design and efficient preparation for novel Copper(II) complexes of N-benzoyl-2-(1H-indol-2-yl)pyrrolidine-1-carbothioamide and determine some of their biological properties.

MATERIALS AND METHODS:

The pyrrolidines based ligands were synthesis from corresponding imine via azomethineylide 1,3-dipolar cycloadditions and aroyl isothiocyanate condensation reactions. The prepared ligands were then treated with appropriate salts of Cu metal which afforded the desired Cu(II) complexes in good to excellent yields. The synthesied compounds were characterized by various analytical techniques. The biological evaluation of prepared compounds were made by using S. aureus (ATCC 25925), E. coli (ATCC 25923), A. baumannii (ATCC 02026), B. subtilis (ATCC 6633), A. hydrophila (ATCC 95080) and M. tuberculosis H37RV

RESULTS:

The Cu (II) complexes were obtained as green solid and the result of biological evaluation shown that the compounds are potential bioactive when tested against anti-TB and the bacteria mentioned above.

CONCLUSIONS:

A simple method was developed to prepare novel Cu (II) complexes based on pyrrolidine and carbothioamide derivatives. The complexes were showing the coordination occur through the sulfur and oxygen atom of carbamothioyl moieties and found to be potential bioactive.

REFERENCES:

1. Piperakis et al., (2011), Molecular Biology International, Reviews, 2011:1-13.
2. Lay et al., (2002), Coordination Chemistry, Reviews,232:95-126.
3. Dondas HA et al,. (2017). Synthesis, 49: 2819–2851.
4. Aly AA. et al., (2007). Journal of Sulfur Chemistry 28(1): 73–93.

P-478: SYNTHESIS, CHARACTERIZATION AND ANTI(MYCO)BACTERIAL ACTIVITY OF THIOESTER DERIVATIVES BEARING BENZAMIDO-2-OXO ALKYL MOIETY

[1] Belveren, S., [1] Poyraz, S., [2] Ulger, M., [1] Dondas, HA.

[1] Mersin University, Department of Analytical Chemistry, Mersin, Turkey

[2] Mersin University, Department of Pharmaceutical Microbiology, Mersin, Turkey

INTRODUCTION:

Thioesters have important preeminent role in the accomplishment of biological, pharmaceutical and industrial processes. Thioesters are the key bioactive compounds in many biosynthetic pathways to fatty acids, esters, polyketides, and nonribosomal peptides. They are also versatile intermediates in food, medicinal and cosmetic chemistry, and in production of new materials (1,2). As part of our previous works (3), we prepared some novel thioester derivatives which can be consider as useful potential bioactive compounds.

MATERIALS AND METHODS:

The novel compounds were prepared from corresponding aroyl isothiocyanate in presence of oximes/imines and characterized by NMR, MS and IR techniques. Anti-TB activity of the tested compound was performed utilizing the resazurin microtitre assay-REMA according to literature method against M. tuberculosis H37Rv strain (4). Isoniazid and ethambutol were used as standard reference drugs. Antibacterial activity of the compound was performed against a range of Gram-positive and Gram-negative bacteria. Ampicillin was used control drug for testing antibacterial activity. (5).

RESULTS:

Some novel thioester derivatives bearing benzamido-2-oxo alkyl moieties were obtained in good to excellent yield and their structure were elucidated. The tested compounds showed potential anti(myco) bacterial activity.

CONCLUSIONS:

A simple method was applied to synthesize the novel thioester derivatives bearing benzamido moiety and showed potential bioactivity when tested against M. tuberculosis H37Rv strain and Staphylococcus aureus (ATCC 25925), Escherichia coli (ATCC 25923), Acinetobacter baumannii (ATCC 02026), Bacillus subtilis (ATCC 6633), Aeromonas hydrophila (ATCC 95080) bacteria.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Mersin University

REFERENCES:

1. Kazemi M, Shiri L (2015). Journal of Sulfur Chemistry, 36(6):613-623.
2. Franke J, Hertweck J (2016). Cell Chemical Biology, 23(10):1179-1192.
3. Dondas et al., (2017). Monatshefte für Chimie, 148:2173-2182.
4. Nateche et al., (2006). Journal of Medical Microbiology, 55:857-860.
5. Gahlaut et al., (2013). Int J Pharm Pharm Sci. 5(2):372-37.

P-479: SYNTHESIS AND ANTICANCER ACTIVITY STUDIES OF SOME NOVEL INDOLE RETINOID DERIVATIVES

[1] Gurkan Alp, AS., [2] Koc, A., [2] Karabay, AZ., [1] Buyukbingol E.

[1] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

[2] Ankara University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey

INTRODUCTION:

The indole ring is an important moiety found in many pharmacologically active compounds with a certain biological activities and its anticancer effectiveness was described in the literature (1). On the other hand, retinoids play essential roles in a variety of physiological processes including mediation of cell growth, differentiation, modulation of apoptosis (2). These properties of retinoids confer a significant therapeutic potential for the treatment of cancer (3). In the present study, we aim to reveal more active and less toxic some novel retinoid compounds consisting of tetrahydronaphthalene ring system which is integrated with substituted indole. For this purpose, novel N-(5-Substituted 1H-indol-1-yl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene-2-carboxamide derivatives (Fig.1) were synthesized and their anticancer effects were determined against the human leukemia cell line HL-60 in vitro.

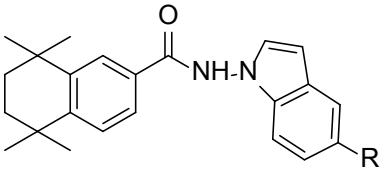


Figure 1. General structure of novel indole retinoid derivatives.

MATERIALS AND METHODS:

The targeted compounds were prepared by using the synthetic procedures described in our previous studies (4,5). Cytotoxic effects of compounds were tested in HL-60 cell line. For this purpose, MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay was performed

RESULTS:

Our results showed that compound 5a and 5b decreased HL-60 cell viability significantly ($p < 0.05$) at different concentrations.

CONCLUSIONS:

In this study, novel retinoid-indole hybride compounds were prepared and evaluated for their in vitro antiproliferative activities against HL-60 AML cells. Compound 5a exhibited remarkable cytotoxic activities. Further research is needed to elicit the mechanisms of their actions on cell viability.

REFERENCES:

1. Sidhu JS, Singla R, et al., (2016). Anticancer Agents Med. Chem., 16:160-173.
2. Niederreither K, Dollé P (2008). Nat. Rev. Genet., 9:541-553.
3. Tang XH, Gudas LJ (2011). Annu. Rev. Pathol., 6:345-364.
4. Gurkan AS, Karabay A, et al., (2005). Arch. Pharm. Chem. Life Sci., 338: 67-73.
5. Gurkan AS, Karabay AZ, et al., (2011). Eur. J. Med. Chem., 46: 468-479.

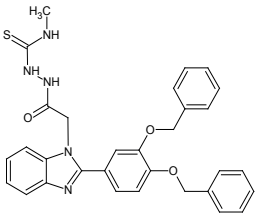
P-480: MOLECULAR DOCKING STUDIES OF SOME NOVEL BENZIMIDAZOLE DERIVATIVES AS EGFR INHIBITORS

Gurkan Alp, AS., Celik, I., Ayhan Kilcigil, G.

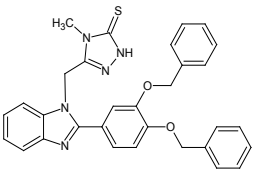
Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

INTRODUCTION:

Epidermal growth factor receptor (EGFR) tyrosine kinase is a member of the human epidermal growth factor receptor family, the overexpression of EGFR is observed in tumors from more than 60% of patients with metastatic non-small cell lung cancer and is correlated with poor prognosis. Therefore, EGFR is an attractive target for anticancer therapy and a larger number of EGFR inhibitors have been developed. Benzimidazoles have various activities and have versatile use in medicinal chemistry, it has been reported that third generation EGFR inhibitor nazartinib, which has benzimidazole structure (1). In this study, docking analysis of novel EGFR inhibitors synthesized were carried out.



16



16c

MATERIALS AND METHODS:

The X-ray structure of EGFR tyrosine kinase (2) in complex with erlotinib was obtained from protein data bank, PDB ID: 1M17. MGL Tools v.1.5.6. (3) was used to prepare the ligands and the receptor. Autodock_ vina v.1.1.2 (4) was used to dock the ligands into the binding site of EGFR. Docked ligands were analyzed with UCSF Chimera-1.7 (5).

RESULTS:

One hydrogen bond (2.26 Å) was observed between C=O of the compound 16 and LYS721 side chain. One hydrogen bond (2.36 Å) was also observed between NH of the triazole ring of the compound 16c and LYS721 side chain. It was shown that 16 and 16c were compatible with the active binding site thanks to van der Waals interactions between the molecule and the residues LEU694, LYS721, PHE699, THR766 in the binding pocket.

CONCLUSIONS:

Docking studies of some novel benzimidazole linked thiosemicarbazide and triazole derivatives were performed by using the X-ray structure of EGFR tyrosine kinase [2]. The docking analysis of the compounds revealed that hydrogen bonding with LYS721 and van der Waals interactions observed in the active site stabilize the molecules in the protein.

REFERENCES:

1. Masuzawa K, Yasuda H et al., (2017). Oncotarget, 8:105479-105491.

2. Stamos J, Sliwkowski MX et al., (2002). J.Biol. Chem., 277:46265-46272.

3. Sanner MF (1999). J.Mol.Graphics Mod., 17:57-61.

4. Trott O, Olson AJ (2010). J.Comp. Chem., 31:455-461.

5. Pettersen EF, Goddard TD et al., (2004). J.Comput. Chem., 25:1605-1612.

P-481: IN VIVO ANTICONVULSANT ACTIVITY AND MOLECULAR MODELING STUDIES OF SOME NEW 1-PHENYL-2-(1H-IMIDAZOL-1-YL)ETHANONE OXIME ESTERS

[1,2] Yurtoglu, S., [1] Sari, S., [1] Sarac, S., [1] Dalkara, S.

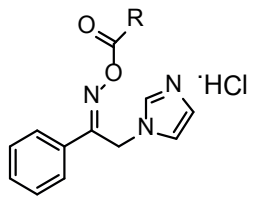
[1] Hacettepe University, Department of Pharmaceutical Chemistry, Ankara, Turkey

[2]Permanent address: Yenisehir Laboratory, Ankara, Turkey

INTRODUCTION:

(Arylalkyl)azoles emerged as a new class of anticonvulsants with nafimidone and denzimol (1). In this study a set of 1-phenyl-2-(1H-imidazol-1-yl)ethanone oxime esters (1-5) were designed, synthesized, and their anticonvulsant activities were evaluated in vivo under the Epilepsy Therapy Screening Program (ETSP) of NIH. Their pharmacokinetic properties and possible anticonvulsant mechanisms were predicted in silico.

Table. Anticonvulsant identification results of 1-5



		6 Hz		MES		Rotorod	
Comp.	R	0.5 h	2 h	0.5 h	2 h	0.5 h	2 h
1	-(CH2)2CH3	300	-	300	300	300	-
2	-CH=CHCH=CHCH3	300	-	300	300	300	-
3	-C6H11	100	300	100	-	300	-
4	-CH=CHC6H5	-	-	300	-	-	-
5	-(CH2)2COC6H5	300	300	300	-	300	-

Results indicate the minimum dose (mg/kg) at which activity or toxicity was observed, "-" means no activity/ toxicity.

MATERIALS AND METHODS:

1-5 were prepared by the reaction of various carboxylic acids with 1-phenyl-2-(1H-imidazol-1-yl) ethanone oxime. Their anticonvulsant identification was performed by the ETSP using 6 Hz, MES, and rotorod test in mice ip. ADMET descriptors were calculated using QikProp and molecular docking was run on Glide (Schrödinger, LLC, NY, 2018) (2) using a GABAAR homology model (3).

RESULTS:

Most of the compounds were found protective against certain seizures induced by 6 Hz and/or MES method. 3 was active in 6 Hz test at 100 mg/kg and 0.5 h (Table). The compounds showed druglikeness and favorable ADMET properties according to the Qikprop calculations. The active compounds showed high affinity binding to the benzodiazepine binding site of GABAAR model making interactions in line with the biological data.

CONCLUSIONS:

1-Phenyl-2-(1H-imidazol-1-yl)ethanone oxime esters proved promising regarding anticonvulsant activity, which might be due to allosteric activation of GABAAR.

ACKNOWLEDGEMENTS:

This study was supported by grants from TUBITAK (SBAG-113S060) and Hacettepe University (014 D09301 001-703, TPT-2015-6794).

REFERENCES:

1. Dalkara S, Karakurt A (2012). Current Topics in Medicinal Chemistry, 12:1033-1071.
2. Friesner RA et al., (2006). Journal of Medicinal Chemistry, 49:6177–6196.
3. Bergmann R et al., (2013). PLoS One, 8:e52323.

P-482: ANTICANCER ACTIVITIES OF NEW SILVER COMPLEXES ON DU-145 HUMAN PROSTATE CANCER CELLS

[1] Sahin Bolukbasi, S.,[2,3] Sahin, N.,[3] Gurbuz, N.,[3] Ozdemir, I.,[1] Cevik, E.,[4] Cummings, BS.

[1]Cumhuriyet University, Faculty of Pharmacy, Department of Biochemistry, Sivas, Turkey

[2]Cumhuriyet University, Faculty of Education Department of Basic Education, Sivas,Turkey

[3]Inonu University, Faculty of Science and Art, Department of Chemistry, Malatya, Turkey

[4]University of Georgia, Faculty of Pharmacy, Department of Pharmaceutical and Biomedical Sciences, Athens, GA, USA

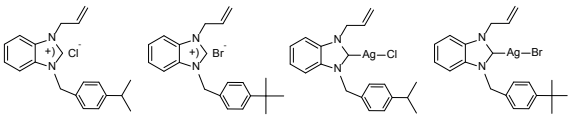
INTRODUCTION:

Cancer is a disease that requires long-term struggle in the material and spiritual direction besides the health problems brought with it. In the world, 14 million people have cancer every year, resulting in the death of 8.2 million people. In the family of metal-NHCs, Ag-NHCs have received a many attention because of their medicinal applications (1). In this study, we aimed to investigate the synthesis, characterization and anticancer activities of two new NHC ligands and their Ag(I) complexes on DU-145 human prostate cancer cells.

MATERIALS AND METHODS:

In this study we synthesized two novel unsymmetrically substituted NHC ligands (1a-b) and their Ag(I) complexes. All new compounds were characterized using elemental analysis, FT-IR, 1H NMR and 13C NMR spectroscopy. Compounds were further evaluated for their in vitro anticancer activities againts on DU-145 prostate cancer cells and L-929

non-cancerous for 24 h, 48 h and 72 h using MTT assay (2).



1a 1b 2a 2b

RESULTS:

In vitro anticancer activitiy assays indicated that these novel compounds showed the dose and time-dependent anticancer activity on DU-145 prostate cancer cells for 24 h, 48 h and 72 h treatment under identical conditions. Further, the ligands (1a-b) and their Ag-complexes (2a-b) had relatively higher cytotoxicity to DU-145 cancer cells than to L-929 non-cancerous cell lines.

CONCLUSIONS:

The in vitro anticancer activity studies indicate that Benzimidazole-Based N-Heterocyclic Carbene(-NHC) ligands and their silver-(I) complexes can inhibit the DU-145 prostate cancer cells proliferation.

ACKNOWLEDGEMENTS:

The authors thank the Scientific and Technological Research of Turkey (TÜBITAK-BIDEB), the National Research Fellow-ship Programme for grants to N.S.

REFERENCES:

1. Hu CQ, Li X, Wang W, Zhang RY, Deng LP (2014). Curr. Med. Chem., 21(10):1220-1230.
2. Skehan P, Storeng R, Scudiero D, Monks A, McMahon J, Vistica D, Warren JT, Bokesch H, Kenney S, Boyd MR (1990). J Natl Cancer Inst., 82(13):1107-1112.

P-483: CYTOTOXIC ACTIVITIES OF NEW NHC COMPOUNDS ON MCF-7 AND MDA-MB-231 HUMAN BREAST CANCER CELLS

[1] Sahin Bolukbasi, S.,[2,3] Sahin, N.,[3] Gurbuz, N.,[3] Ozdemir, I.,[1] Cevik, E.,[4] Cummings, BS.

[1]Cumhuriyet University, Faculty of Pharmacy, Department of Biochemistry, Sivas, Turkey

[2]Cumhuriyet University, Faculty of Education Department of Basic Education, Sivas,Turkey

[3]Inönü University, Faculty of Science and Art, Department of Chemistry, Malatya, Turkey

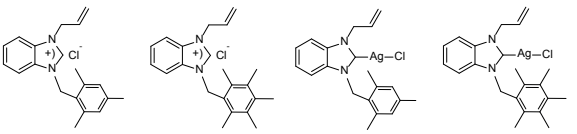
[4]University of Georgia, Faculty of Pharmacy, Department of Pharmaceutical and Biomedical Sciences, Athens, GA, USA

INTRODUCTION:

Breast cancer represents the most commonly diagnosed cancer and the leading cause of cancer death in women worldwide, with approximately 1.7 million cases (25% of all cancers) and 521,900 deaths recorded in 2012 (1). Recently, Ag-N-heterocyclic carbene (NHC) complexes appeared as an emerging field of research in medicinal chemistry (2). In this study, we aimed to investigate the synthesis, characterization and cytotoxic activities of two new benzimidazole-based NHC ligands and their Ag(I) complexes on breast cancer cells.

MATERIALS AND METHODS:

In this study, two new NHC ligands (1a-b) and their Ag(I)-NHC complexes (2a-b) has been synthesized and characterized by elemental analysis, FT-IR, 1H NMR and 13C NMR spectroscopies. The cytotoxic activities of compounds were tested againts on MCF-7, MDA-MB-231 human breast cancer cells and L-929 non-cancerous cells for 24 h, 48 h, 72 h using the MTT assay and determined IC50 concentrations for the compounds (3).



1a 1b 2a 2b

RESULTS:

The results showed that ligands and Ag(I)-NHC complexes exhibited cytotoxic activity against tested cell lines to a different degree. The cytotoxicity of the compounds were found to be concentration and time dependent. In addition, additional CH3 group in benzene ring increases the anticancer activity of the complexes.

CONCLUSIONS:

In vitro cytotoxicity assays indicated that these novel compounds showed the dose and time-dependent cytotoxic activity on breast cancer cells. The ligands (1a-b) and their Ag-complexes (2a-b) are more cytotoxic on breast cancer cell line than L-929 healthy cells.

ACKNOWLEDGEMENTS:

The authors thank the Scientific and Technological Research of Turkey (TÜBITAK-BIDEB), the National Research Fellow-ship Programme for grants to N.S.

REFERENCES:

1. Ferlay J, Soerjomataram I, Dikshit R et al., (2012). Int. J. Cancer. 136(5). E359-86
2. Asif M, Iqbal, MA, Hussein MA, Oon CE, Haque RA, Khadeer Ahamed MB, Abdul Majid AS, Abdul Majid AMS (2016). European journal of medicinal chemistry. 108:177-187.
3. Skehan P, Storeng R, Scudiero D, Monks A, McMahon J, Vistica D, Warren JT, Bokesch H, Kenney S, Boyd MR (1990). J Natl Cancer Inst. 82(13):1107-1112.

P-484: SYNTHESIS, STRUCTURAL IDENTIFICATION OF NOVEL INDOL-THIAZOLIDINEDIONE DERIVATIVES

Baran, S., Zengin, F., Ates Alagoz, Z.

Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

INTRODUCTION:

As part of an ongoing program aimed at recognizing novel antioxidant, antimicrobial, and anticancer molecules, herein we designed and synthesized new indole-thiazolidinedione derivatives as antimicrobial agents. Previously, we reported that synthesis and antimicrobial activity of new tetrahydro-naphthalane-thiazolidinedione derivatives. Some of our compounds showed equal and /or greater antimicrobial activity against MRSA and EC than ampicillin and sultamicillin. To provide more effective therapeutic agents with the beneficial effects of indole rings but reduced side effects, we developed conformationally constrained indole moiety, which is integrated with thiazolidinedion ring system.

MATERIALS AND METHODS:

Syntheses of the compounds were carried out starting from chloro acetic acide and thiourea to give thiazolidinedione(1). This was followed by reaction with potassium hydroxide to get potassium salt. Due to the labile hydrogen atom at the 3-position, the thiazolidine2,4-dione was N-alkylated with appropriate phenacyl halides in alkaline medium(2). The condensation of N-phenacyl intermediates with indole carboxaldehydes in methanol and in the presence of diethanol amine led to 5-(5-substitue-1H-Indol-3-ylmethylene)-3-(2-oxo-2-substituephenyl-ethyl)-thiazolidine-2,4-dione derivatives.

RESULTS:

5-(5-substitue-1H-Indol-3-ylmethylene)-3-(2-oxo-2-substituephenyl-ethyl)-thiazolidine-2,4-dione derivatives were synthesized. Purity control and structural elucidation were controlled by using elemental analyser and 1H, 13C-NMR, Mass spectrometers, respectively.Due to the labile hydrogen atom at the 3-position, the thiazolidine-2,4-dione was N-alkylated with appropriate phenacyl.

CONCLUSIONS:

Future studies will include testing antimicrobial activities of the synthesized compounds for their in vitro growth inhibitory activity against different bacteria and yeasts, and also determination of the minimal inhibitory concentration (MIC) of the compounds by the tube dilution technique. In order to improve the antimicrobial activity, chemical synthesis of additional indole-thiazolidinedione derivatives are warranted.

REFERENCES:

1. Tuncbilek M, Altanlar N (2006). Arch. Pharm. Chem. Life Sci, 339:213-216.
2. Ates Alagoz Z, Altanlar N, Buyukbingol E (2009). J. Heterocyclic Chem., 46 (6):1375-1379.

P-485: DESIGN, SYNTHESIS AND MAO ENZYMES INHIBITORY ACTIVITY EVALUATION OF NEW BENZOTHIAZOLE-THIAZOLYLHYDRAZINE DERIVATIVES

[1,2] Levent, S., [1,2] Acar Cevik, U., [1,2] Saglik, BN., [1,2] Ozkay, Y., [1] Kaya Cavusoglu, B., [1] Kaplancikli, ZA., [3] Korkut, B., [1,2] Osmaniye, D.

[1]Anadolu Universty, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskişehir, Turkey

[2]Anadolu Universty, Faculty of Pharmacy, Doping and Narcotic Compounds Analysis Laboratory Eskişehir, Turkey

[3]Anadolu Universty, Faculty of Pharmacy, Department of Pharmaceutic Toxicology Eskişehir, Turkey

INTRODUCTION:

Monoamine oxidase (MAO) possess two isoforms recognized as MAO-A and MAO-B and it plays an important role in the metabolism of endogenous and exogenous amines (1,2). The previous studies have displayed that benzothiazole derivatives have potent MAO enzymes inhibitor activity (3). Additionally, thiazolylhydrazine derivatives are frequently used due to their MAO enzyme inhibitor activities (4). Information of MAO enzyme inhibitor activities in both scaffolds (benzothiazole and thiazolylhydrazine) has prompted interest about the MAO enzyme inhibitor effects of compounds including these two scaffolds. Consequently, within the scope of this study, a series of new benzothiazole-thiazolylhydrazine derivatives were synthesized as MAO enzyme inhibitor.

MATERIALS AND METHODS:

In this study, benzothiazol-2-yl-N-(4-phenylthiazol-2-yl) benzohydrazonothioate was synthesized and 14 final compounds were obtained by derivatizing ortho and para position of phenyl directly bonded to thiazole ring. The structures of the synthesized compounds were elucidated using FT-IR, 1H-NMR, 13C-NMR, and HRMS spectral data. The inhibitory activity of the obtained compounds against hMAO-A and hMAO-B enzymes was evaluated by using in vitro Amlex Red® reagent based fluorometric method (5).

RESULTS:

Most of the obtained compounds displayed important inhibition against MAO enzymes.

CONCLUSIONS:

According to results of activity studies, it is obvious that the benzothiazole-thiazolylhydrazine derivatives are potent monoamine oxidase inhibitors

REFERENCES:

1. Binda C, Wang J et al., (2007). Journal of Medicinal Chemistry, 50:5848-5852.
2. Carradori C, Silvestri R et al., (2015). Journal of Medicinal Chemistry, 58:6717-6732.
3. Ilgin S, Osmaniye D et al., (2017). Molecules, 22:2187
4. Chimenti P, Petzer A et al., (2013). European Journal of Medicinal Chemistry, 66:221-227.
5. Can ÖD, Osmaniye D et al., (2017). European Journal of Medicinal Chemistry. 131:92-106.

P-486: SYNTHESIS, CHARACTERIZATION AND ANTI-BIOFILM ACTIVITY STUDIES ON NOVEL UREA/THIOUREA DERIVATIVES

[1] Turk, S., [1] Tok, F., [2] Ulusoy, S., [1] Karakus, S., [1] Kocyigit Kaymakcioglu, B., [3] Bosgelmez Tinaz, G.

[1]Marmara University, Department of Pharmaceutical Chemistry, Istanbul, Turkey

[2]Suleyman Demirel University, Department of Molecular Biology, Isparta, Turkey

[3]Marmara University, Department of Basic Sciences, Istanbul, Turkey

INTRODUCTION:

The discovery of antibiotics made it possible to treat the infectious diseases that were once untreatable and enabled to save millions of lives by taking many dangerous bacterial infections under control. However, with the occurrence of bacterial resistance and in regard to the increasing incidence of multidrug resistance in pathogenic bacteria, the identification of alternative antimicrobial drug targets to develop novel treatment strategies have become a necessity. One such new strategy is the disruption of bacterial quorum sensing (QS) system. By using this system, in an attempt to develop potent anti-biofilm agents, herein we represented the synthesis, characterization and anti-biofilm activities of novel urea/thiourea derivatives.

MATERIALS AND METHODS:

The final compounds were obtained by the reaction of gabapentine with different isocyanates/ isothiocyanates and tested for their quorum sensing inhibitory (QSI) capacity using quorum sensing inhibitor selector 1 (QSIS1) bioassay (1,2).

RESULTS:

The structures of the compounds were characterized by various spectroscopic methods (IR, 1H-NMR, 13C-NMR, MS), besides elemental anaysis. Additively, their anti-biofilm activity was examined by using the QS system which has been shown to control production of an array of extracellular virulence factors and the formation of biofilm in a variety of bacterial pathogens including Pseudomonas aeruginosa (3).

CONCLUSIONS:

In summary, a new series of urea/thiourea derivatives have been successfully synthesized starting from [1-(aminomethyl)cyclohexyl]acetic acid, their structures were elucidated and finally they were evaluated as potential anti-biofilm agents.

ACKNOWLEDGEMENTS:

This study was supported by the Marmara University Scientific Reseach Comittee (Project No: SAG-A-060911-0277)

REFERENCES:

1. Turk et al., (2017). Marmara Pharmaceutical Journal, 21:89-95.
2. Jatav et al., (2008). European Journal of Medicinal Chemistry, 43:135-141.
3. Hentzer M, Givskov M (2003). The Journal of Clinical Investigation, 112:1300-1307.

P-487: SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF NOVEL ETHER-LINKED DERIVATIVES OF ORNIDAZOLE

[1] Senkardes, S., [1] Kulabas, N., [2] Kalayci, S., [2] Sahin, F., [1] Kucukguzel, I., [1] Kucukguzel, SG.

[1]Marmara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, İstanbul, Turkey

[2]Yeditepe University, Faculty of Engineering and Architecture, Department of Genetics and Bioengineering, İstanbul, Turkey

INTRODUCTION:

Today, a great number of antibiotics and synthetic drugs are used in clinic for the treatment of commonly occurring microbial infections. But along with their widespread use, the emergence of multidrug-resistant strains of pathogens reduce the efficacy of these drugs. Imidazole nucleus, which exhibit a wide range of medicinal potential, is a quite important heterocycle for drug design due to its ability to readily interact with diverse biological targets such as DNA, receptors and critical enzymes (1). Ornidazole is a chiral 5-nitroimidazole class antimicrobial agent and used for the prophylaxis and treatment of susceptible protozoal and anaerobic bacterial infections (2). In this study, new ether linked ornidazole derivatives were designed, synthesized and characterized for evaluation of their antimicrobial activity, since imidazole-containing derivatives exhibit various biological activities and pharmacological properties including antimicrobial activity (3).

MATERIALS AND METHODS:

All solvents and reagents were obtained from commercial sources and used without purification. For antimicrobial activity, the sensitivity of the bacterial strains towards the compounds was evaluated from

the minimal inhibitory concentration (MIC) and zone diameter (mm) values obtained by the micro-well dilution and disk diffusion methods. The antibacterial activity of the compounds were evaluated against 6 cultures. The microorganisms used were Escherichia coli ATCC 10536, Staphylococcus aureus ATCC 6538, Pseudomonas aeruginosa ATCC 15442, Bacillus subtilis ATCC 6633, Candida albicans ATCC 10231 and Aspergillus niger ATCC 16404. Antimicrobial activity tests were performed according to previous methods (4,5).

RESULTS:

Ornidazole, 1-(3-chloro-2-hydroxypropyl)-2-methyl-5-nitroimidazole was reacted with various phenolic compounds using acetonitrile as a solvent in order to obtain new ether-linked derivatives. Characterization of the synthesized compounds were achieved by the elemental analysis, IR, 1H-NMR and mass spectral data while their purities were proved by TLC and HPLC. According to biological evaluation findings, most of the compounds have significant antimicrobial activity, especially 1-(2-methyl-5-nitro-1H-imidazol-1-yl)-3-(4-nitrophenoxy)propan-2-ol and 1-(4-chloro-3-methylphenoxy)-3-(2-methyl-5-nitro-1H-imidazol-1-yl) propan-2-ol showed best activity against Bacillus subtilis with MIC values of 4mg/ml.

CONCLUSIONS:

In the present research, we aimed at obtaining new 1-(2-methyl-5-nitro-1H-imidazol-1-yl)-3-(substituted phenoxy)propan-2-ol derivatives as potential antimicrobial agents which were synthesized from ornidazole. As conclusion, the synthesized compounds have been exhibited moderate to high activities against Bacillus subtilis.

REFERENCES:

1. Wen et al., (2016). Bioorganic and Medicinal Chemistry Letters, 26:2768-2773.
2. Singh et al., (2003). Profiles of Drug Substances, 30:123-184.
3. Kim et al., (2013). Bioorganic and Medicinal Chemistry Letters, 23:4315-4318.
4. Kalaycı et al., (2016). Infectious Disorders - Drug Targets, 16:44-53.
5. Kalaycı et al., (2014). Current Psychopharmacology, 3:195-202.

P-489: ANTIBACTERIAL SCREENING OF AN IN-HOUSE AZOLE OXIME ESTER LIBRARY

[1] Sari, S., [2] Kart D., [3] Karakurt, A.,[1] Sarac, S., [1] Dalkara, S.

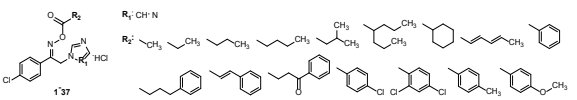
[1] Hacettepe University, Department of Pharmaceutical Chemistry, Ankara, Turkey

[1] Hacettepe University, Department of Pharmaceutical Microbiology, Ankara, Turkey

[1] Inonu University, Department of Pharmaceutical Chemistry, Malatya, Turkey

INTRODUCTION:

Azoles are a rare class of antibiotics used against some anaerobes and parasites (1). Some (arylalkyl) azoles in oxime ether structure were previously reported to show potent antibacterial effects (2). Thus, we performed antibacterial testing of an in-house library made up of 37 compounds in 1-(2,4-dichlorophenyl)-2-(1H-imidazol/1,2,4-triazol-1-yl)ethanone oxime ester structure in order to find new hits.



MATERIALS AND METHODS:

Synthesis of 1-37 was previously reported (3). Their minimum inhibitor concentration (MIC) values were determined against ATCC strains of Staphylococcus aureus, Enterococcus faecalis, Pseudomonas aeruginosa, and Escherichia coli using Broth microdilution method according to the Clinical & Laboratory Standards Institute (CLSI) guidelines (4). Ciprofloxacin and gentamicin were used as positive controls.

RESULTS:

Most of the compounds showed growth inhibition against the tested bacteria although their MIC values were higher than the reference drugs. Compound 4, 12, and 14 were the most potent with a MIC value of 64 µg/mL.

CONCLUSIONS:

Although less potent than the reference drugs, 1-(2,4-dichlorophenyl)-2-(1H-imidazol/1,2,4-triazol-1-yl)ethanone oxime esters proved promising antibacterial compounds for the future studies.

ACKNOWLEDGEMENTS:

This study was supported by grants from TUBITAK (SBAG-113S060) and Hacettepe University (TDK-2017-14965, TPT-2015-6794, TPT-2018-16666).

REFERENCES:

1. Mital A (2009). Scientia Pharmaceutica, 77(3):497–520.
2. Karakurt A et al., (2001). European Journal of Medicinal Chemistry 36:421–433.
3. Sari S et al., (2017). Archiv der Pharmazie 350: e201700043.
4. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically: Approved Standard, 8th ed., M07-A8. Clinical and Laboratory Standards Institute, Wayne, PA, 2008

P-490: SYNTHESIS AND CYTOTOXIC ACTIVITY OF SOME QUINOXALINE DERIVATIVES

[1] Soyer , Z., [1] Uysal, S., [1] Tarikogulları, AH.,[2] Ilhan, R., [2] Kirmizibayrak, PB.

[1] Ege University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Izmir, Turkey

[2] Ege University, Faculty of Pharmacy, Department of Biochemistry, Izmir, Turkey

INTRODUCTION:

Quinoxaline which is one of the Heterocyclic rings containing nitrogen exhibits a broad spectrum of biological activity such as antimicrobial, antiviral and anticancer (1). It may act as bioisostere of both pteridine and quinazoline rings present in the most representative drugs as methotrexate, trimetrexate and tomude (2). On the other hand, literature survey revealed that hydrazone moiety has significant role as antitumoral activity which makes it important for the anticancer drugs (3). In the light of these facts, a series of quinoxaline derivatives were synthesized and evaluated for their cytotoxic activity against A549, U2OS, HeLa and 293T cell lines.

MATERIALS AND METHODS:

2,3-dihydroxyquinoxaline, 2,3-dichloroquinoxaline and 2 different quinoxaline dedicated with heterocyclic rings substituted to hydrazone derivatives (Figure 1) were prepared following the procedure (4). Structures of the target compounds were verified by spectral analysis. Cytotoxic activities of the compounds were determined by WST-1 cell proliferation assay. Doxorubicin was used as positive control.

RESULTS:

All synthesized compounds exhibited cytotoxic activity with comparable IC50 values against tested cell lines, In general, all synthesized compounds have lower cytotoxic activity than the reference drug doxorubicin. Compound 2 was the most active against U2OS cell line.

CONCLUSIONS:

Our preliminary activity screening results have demonstrated that this class of quinoxaline derivatives has cytotoxic activity and can be a promising structure for further studies.

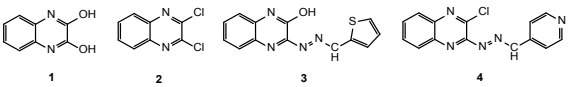


Figure 1

ACKNOWLEDGEMENTS:

This study was supported by research grant from Ege University (Project Number: 16-ECZ-013)

REFERENCES:

1. Pereira et al., (2015). European Journal of Medicinal Chemistry, 97:664-672.
2. Galal et al., (2011). European Journal of Medicinal Chemistry, 46:327-340.
3. Nasr, T., Bondock, S., Youns, M (2014). European Journal of Medicinal Chemistry, 76:539-549.
4. Noorulla, S., Sreenivasulu, N (2011). Interntional Journal of Pharmaceutical Sciences and Research, 2(9):2337-2342.

P-491: DESIGN, SYNTHESIS AND BIOLOGICAL ACTIVITY STUDY OF DISUBSTITUTED 1,3,4-OXADIAZOLE DERIVATIVES

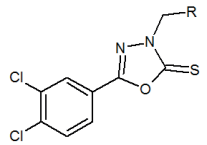
[1] Ozyazici, T., [2] Sahin, F., [1] Koksal, M.

[1] Yeditepe University, Faculty of Pharmacy, Departmant of Pharmaceutical Chemistry, Istanbul, Turkey

[2] Yeditepe University, Faculty of Engineering and Architecture, Departmant of Genetics and Bioengienering, Istanbul, Turkey

INTRODUCTION:

Infectious diseases remain a major worldwide health problem due to the rapid development to the existing antimicrobial drugs. The increasing of usage or misusage of the existing antimicrobial drugs have resulted in the development of resistant pathogens (1, 2). Recent studies reflect that considerable antibacterial and antifungal activity had been exhibited by 1,3,4-oxadiazole structure and in this experiment pharmaceutically active 1,3,4-oxadiazole ring is suitably substituted with piperidine derivatives from its spesified positions with modified organic reaction mechanisms. Motivated by the previous studies, we are purposed to investigate the antibacterial and antifungal activity of our newly synthesized compound series.



R: Substituted piperidine derivatives

MATERIALS AND METHODS:

The synthetic pathway was started with Fischer esterification of substituted benzoic acid in acidic media with alcohol and resulted ester functional group was converted to acid hydrazide with hydrazine hydrate. Produced hydrazid group was cyclized with carbon disulfide and potassium hydroxide to obtain main structure. For the last step by using Mannich reaction procedure; substitutedpiperidine derivatives and oxadiazole ring were combined with methylene bridge (3). For biological activity; derived compounds were screened for their antimicrobial performance against a series of bacteria and fungus by disc-diffusion method.

RESULTS:

Synthesized compounds were characterized by IR, 1H-NMR , 13C-NMR and all of them gave satisfactory analytical and spectroscopic data which were in full accordance with their depicted structure. The molecular structures were confirmed on the basis of their spectral data and the purity was checked by elemental analysis. Most of them were displayed variable inhibitory effects on the growth of microorganisms.

CONCLUSIONS:

A total analysis of the antibacterial, antifungal and antiyeast activity revealed that new structures were showed severe activity against Bacillus cereus, Bacillus ehimensis and Bacillus thuringiensis species according to oflaxacin and these observations may promote a further development through structural modification of 1,3,4-oxadiazole from different position-derivative combinations in which may result as better antimicrobial activity on more species.

REFERENCES:

1. Nagai K, et al., (2002). Antimicrobial Agents Chemotheraphy 46:1273-1280.
2. 2.Pfeltz RF, Wilkinson BJ (2004). Current Drug Targets: Infectious Disorders 4: 273-294.
3. 3.Manjunatha K., et al., (2010). European Journal of Medicinal Chemistry 45:5225-5233.

P-492: DETERMINATION OF RISPERIDONE AND 9-HYDROXYRISPERIDONE IN HUMAN PLASMA BY LC-MS

[1] Altuntas, TG., [2] Demiray Yıldırım, G.

[1] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

[2] Turkish Medicines and Medical Devices Agency, Ankara, Turkey

INTRODUCTION:

Risperidone, 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4H-pyrido [1,2- a] pyrimidin-4-one), is an antipsychotic agent used for the treatment of both positive and negative symptoms of schizophrenia. Its effects is observed by blocking seratonin 5-HT2 and dopamine D2 receptors (1,2). Risperidone is mainly metabolized in the liver by cytohrome p450 isoenzymes (CYP2D6) to main metabolite of risperidone, 9-hydroxyrisperidone which has a similar pharmacological activity as the parent compound. For adequate support of clinical studies with risperidone, an analytical method is required for the determination of plasma levels of both risperidone itself and its active metabolite 9-hydroxyrisperidone.

MATERIALS AND METHODS:

The chromatographic separation was performed on a Sunfire C18 analytical column at a temperature of 25 ºC. The mobile phase was ammonium acetate: acetonitrile (60:40 v/v) with 0.15 mlmin-1 flow rate and injection volume of sample was 20 µl.

RESULTS:

In these conditions retention times for risperidone, 9-hydroxyrisperidone and the IS were approximately 1.46 min., 1.32 min. and 2.68 min., respectively and the total run time was 6 min. The analytes were ionized in the positive electrospray ionization ion source (ESI+) of the mass spectrometer in the selected ion monitoring mode (SIM). Risperidone, 9-hydroxyrisperidone and the internal standard quetiapine fumarate were identified at m/z 411, 427, and 384, respectively.

CONCLUSIONS:

A simple and sensitive LC-MS method for the determination of risperidone and 9-hydroxyrisperidone in human plasma has been developed and validated.

ACKNOWLEDGMENTS

The authors would like to thank Novagenix Ar-Ge Research Center, Ankara-Turkey.

REFERENCES:

1. Leysen JE, Gommeren W et al., (1988) J. Pharmacol. Exp. Ther, 247:661-670.
2. Grant S, Fitton, A (1994). Drugs 48:253-273.

P-493: SYNTHESIS, CHARACTERIZATION AND ANTIFUNGAL EVALUATION OF BENZAZOLE DERIVATIVES

[1,2] Acar Cevik, U., [1,2] Saglik, BN., [1,2] Levent, S., [1,2] Osmaniye, D., [1,2] Ozkay, Y., [1] Kaplancikli, ZA., [3] Korkut, B., [1] Kaya Cavusoglu, B.

[1]Anadolu Universty, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskişehir, Turkey

[2]Anadolu Universty, Faculty of Pharmacy, Doping and Narcotic Compounds Analysis Laboratory, Eskişehir, Turkey

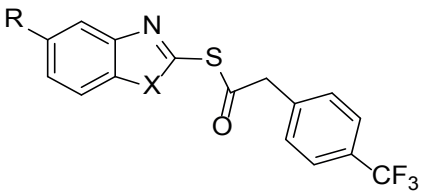
[3]Anadolu Universty, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Eskişehir, Turkey

INTRODUCTION:

The incidence of infection by opportunistic and pathogenic fungi has been increasing in recent years (1).Currently, the available antifungal agents to treat fungal infections can be divided into four categories based on their mode of action, including the polyenes, echinocandins, azoles, and antimetabolites. Clinically, representative antifungal drugs have certain limitation such as, narrow spectrum of activity and the emergence of drug resistance (generally azoles). Therefore, there is an urgent need for development of antifungal agents of new molecular scaffolds with high efficiency, broad spectrum and optimal pharmacokinetics are highly desirable (2,3).

MATERIALS AND METHODS:

Target compounds (2a-2j) were synthesized via reaction of 2-bromo-4'-trifluoromethylacetophenone and corresponding mercaptobenzazole. Antifungal activity studies were performed according to EUCAST definitive method (EDef 7.1) (4).



RESULTS:

Synthesized compounds showed antifungal activity against Candida species to different rates. In the series, compound 2i was the most active derivative that displayed noncytotoxicity.

CONCLUSIONS:

The synthesized compounds displayed promising antifungal activity compared to the standard drugs. We expect that findings of the present study may have an effect on medicinal chemists to discover more active anticandidal compounds in further studies.

REFERENCES:

1. Shi C, Liu C, et al., (2015). Mycopathologia, 180:203-207.
2. Shaikh MH, Subhedar DD, et al., (2016). Journal of Heterocyclic Chemistry, 54:413-421.
3. Cagri Karaburun A, Kaplancikli ZA, et al., (2011). Letters in Drug Design Discovery, 8: 811-815.
4. EUCAST. Definitive Document EDef 7.1: Method for the Determination of Broth Dilution MICs of Antifungal Agents for Fermentative Yeasts.

P-494: INVESTIGATION OF SOME 3-ARYL AMINE 2-METHLY-SUBSTITUTED 3H-QUINAZOLIN-4-ONES IN VITRO ANTIMICROBIAL EFFECT AND CYTOTOXICITY ON HUMAN GINGIVAL FIBROBLASTS

[1] Demirel, UU., [2] Yilmaz, A., [3] Arslan, U.

[1] Altınbaş University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Istanbul, Turkey

[2] Selçuk University, Faculty of Science, Department of Chemistry, Konya, Turkey

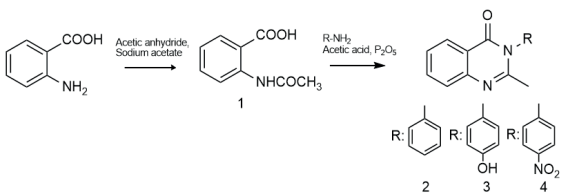
[3] Selçuk University, Faculty of Medicine, Department of Biochemistry, Konya, Turkey

INTRODUCTION:

Quinazolinones are important compounds possessing wide range of biological applications. Some of these could be list as antimalarial, anticonvulsant, anti-inflammatory and analgesic agents, antiviral, CNS depressant, antimicrobial(1). The aim of this study is to synthesize and investigate antimicrobial and cytotoxic activity of derivatives of 2-metil-3H-quinazolinone, which are 2-metil-3-fenil-3,4-dihidrokinazolin-4-on (2), 2-metil-3(4-hidroksifenil)-3,4-dihidrokinazolin-4-on (3), 2-metil-3(4-nitrofenil)-3,4-dihidrokinazolin-4-on (4), compounds.

MATERIALS AND METHODS:

Compounds 1-4 have been prepared according to the published methods (2).



All compounds were characterized via infrared, 1H-NMR, 13C-NMR, elemental and mass spectral analysis. In antimicrobial activity studies were used microdilution methods. In this study, the compounds 2-4 were examined antimicrobial activity against some selected Gram-negative and Gram-positive bacteria and compared with commercial antibiotics. The compounds were screened for their antimicrobial

activity in vitro against *E. faecalis* ATCC 29212, *P. aeruginosa* ATCC 27853, *S. aureus* ATCC 29213, *E. Coli* ATCC 25922 bacteria and compared with commercial antibiotics (Ampicillin and Gentamicin). Effects of compounds on the proliferation of gingival fibroblasts observed. Cells were examined for 88h using a real-time cell analyzer.

Results:2 and 4 showed the lowest MIC value (64 µg/mL) against Pseudomonas aeruginosa strain and this value is higher than the gentamicin but lower than ampicillin. Clear cytotoxic effects on proliferation of the gingival fibroblasts were observed in 3 and 4 chemical substance applications immediately after treatment when compared to the control group

CONCLUSIONS:

MIC value (128 µg/mL) of compounds 3 against Pseudomonas auriginosa is the same as with ampicillin, while the MIC value (64 µg/mL) of compounds 2, and 4 is lower than ampicillin.

REFERENCES:

1. Desai NC, Dodiya A, Shihory N (2013). Journal of Saudi Chemical Society, 17:259-267.
2. Meyyanathan SN, Ramu M, Suresh B (2010). Medicinal Chemistry Research, 19:993-999.

P-496: SYNTHESIS OF NOVEL SCHIFF BASE DERIVATIVES AND EVALUATION OF THEIR MONOAMINE OXIDASE INHIBITORY ACTIVITY

[1] Pirincci, Y., [1] Tok, F., [1] Kocyigit-Kaymakcıoglu, B., [2,3] Levent, S., [2,3] Kaplancikli, ZA.

[1] Marmara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Istanbul, Turkey

[2] Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry,Eskişehir, Turkey

[3] Anadolu University, Faculty of Pharmacy, Doping and Narcotic Compounds Analysis Laboratory, Eskişehir, Turkey

INTRODUCTION:

Monoamine oxidase (MAO) enzymes have been crucial targets in drug design for the treatment of psychiatric and neurological disorders (1). MAO-A inhibitors are clinically used mostly as antidepressants (2) whereas MAO-B inhibitors are generally used in dealing with symptoms associated with Parkinson's and Alzheimer's diseases (3). Despite their long clinical success, first-generation MAO inhibitors have several problems including interactions with other drugs and tyramine, which is a dietary amine and may cause a fatal hypertensive crisis. In view of these adverse actions and restrictions, the clinical use of first generation of MAO inhibitors have been decreased whereas second generation MAO inhibitors such as selegiline and moclobemide have come into prominence due to lack of above problems. In view of information mentioned above, researchers have shown an increased interest in developing novel and potent MAO inhibitors. In the light of above information, herein we report the synthesis and MAO inhibitory activity of some novel pyrazolinone derivatives.

MATERIALS AND METHODS:

The structure confirmation of the synthesized compounds was performed using FT-IR, 1H-NMR, 13C-NMR, and HRMS spectral data. Their inhibitory activity of the final compounds against hMAO-A and hMAO-B enzymes was evaluated by using in vitro Amplex Red® reagent based fluorometric method (4). Docking studies were carried out by using Schrödinger Maestro interface (5) to view the binding modes of most potent derivative in the enzyme active site.

RESULTS:

According to the enzyme inhibitory studies, enzyme inhibition profile of the synthesized compounds against MAO-B enzyme were better than those of MAO-A enzyme. So, it was shown that compounds displayed MAO-B inhibition selectivity. Among the series, ANT-13 was found as the most active derivative with IC50 value of 0.0489 ±0.0016 µM. Docking studies have shown that this derivative is well placed in the active site of the enzyme.

CONCLUSIONS:

Consequently, synthesized compounds have been found as selective MAO-B inhibitors and some of final compounds displayed potent inhibition profile.

REFERENCES:

1. Ramsay RR, (2012). Current Topics in Medicinal Chemistry, 12:2189-2209.
2. Legoabe L, Petzer A et al., (2015). Drug Design, Development and Therapy, 9:3635-3644.
3. Checkoway H, Franklin GM et al., (1998). Neurology, 50:1458-1461.
4. Can NÖ, Osmaniye D et al., (2018). European Journal of Medicinal Chemistry, 144:68-81.
5. Maestro, version 10.6, Schrödinger, LLC, New York, NY, 2016.

P-497: SYNTHESIS AND CHARACTERIZATION OF SOME NEW 6-SUBSTITUTED BENZOXAZOLINONEDERIVATIVES

Mulazim, Y. , Kesanli, B.

Near East University, Department of Pharmaceutical Chemistry, Nicosia, North Cyprus

INTRODUCTION:

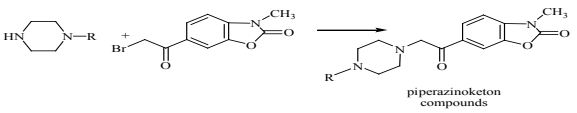
2(3H)-Benzoxazolone derivatives are considered ideal scaffolds for synthesis of drug candidates (1). They have been of interest in medicinal chemistry since they are readily available, affordable, susceptible to chemical modifications and most importantly exhibit wide range of biological activities. Their pharmacological activities include antibacterial, antifungal, analgesics-antiinflammatory,anti-nociceptive, antiulcer, anticancer, and anti-HIV (2-3).

MATERIALS AND METHODS:

All chemicals and reagents were obtained from Sigma Aldrich Chemical Co. or Riedel Chemical Co. and were used without further purification. The FT-IR spectra of the compounds were recorded on a Perkin Elmer Spectrum 100 spectrophotometer with attenuated total reflection (ATR) (in wave numbers) in cm-1. The 1H and 13C NMR spectra of the compounds were recorded on a Mercury Varian 400 MHz NMR Spectrometer using deuterated chloroform (CDCl3) as solvent. Chemical shifts (δ) values were reported in parts per million (ppm).

RESULTS:

We have already synthesized and characterization of two sets of 6-acyl-2(3H)-Benzoxazolone derivatives. One is piperazino ketone family and the other is the reduced form, piperazino ethanol family. General structures of these molecules are given below.



R = 2-(pyrimidyl), 1-Naphthylmethyl, Diphenylmethyl, 2-Furoyl, 2,5-Dimethylphenyl, 2-Methylbenzyl, 4-bromophenyl, 4-Nitrophenyl

CONCLUSIONS:

In conclusion, we have synthesized 6-acyl substituted 2(3H)-Benzoxazolinone derivatives. The antimicrobial studies ongoing at Microbiology Laboratories at Near East University Hospital.

REFERENCES:

1. Poupaert J, Carato P, Colacino E. (2005) Curr. Med. Chem.12: 877-885.
2. Şafak C, Erdoğan H, Palaska E, Sunal R, Duru S. (1992) J. Med. Chem. 35: 1296-1299.
3. Mulazim, Y., Berber, C., Erdogan, H., Ozkan,M. H.,Kesanli.(2017)TheEuroBiotech Journal. 1: 235-240.

P-498: SYNTHESIS AND ANTICANCER ACTIVITY POTENTIAL OF BIS(1,3,4-THIADIAZOLE) DERIVATIVES

[1,3] Ozkay, Y., [1,3] Osmaniye, D., [1] Kaya Cavusoglu, B., [1,3] Saglik, BN., [1,3] Levent, S., [1,3] Acar Cevik, U., [2] Atli, O., [1] Kaplancikli, ZA.

[1] Anadolu University, Department of Pharmaceutical Chemistry, Eskisehir, Turkey

[2] Anadolu University, Department of Pharmaceutical Toxicology, Eskisehir, Turkey

[3] Anadolu University, Doping and Narcotic Compounds Analysis Laboratory, Eskisehir, Turkey

INTRODUCTION:

Cancer is still a prominent public health problem which is characterized by the uncontrolled cellular proliferation and invasion to other parts of the body. Although the treatment of cancer comprises surgery, chemotherapy and radiotherapy, the main approach is chemotherapy which is more common, easy and practicable. However, low bioavailability, toxicity and non-selective nature of anticancer drugs and drug-resistance are certain obstacles that limit their usage (1,2). Therefore, the identification of novel, more potent, selective, and less toxic antitumor agents is a vital need. Diverse bis(1,3,4-thiadiazole) derivatives have exhibited anticancer activity (3). Some studies showed that 1,3,4-thiadiazole compounds have been reported to act through many mechanisms including caspase activators, tyrosine kinase inhibitors, carbonic anhydrase inhibitors (4). In this present study, some novel bis(1,3,4-thiadiazole) derivatives were synthesized and their potential anticancer activities were examined.

MATERIALS AND METHODS:

The cytotoxicity of the compounds was evaluated against some tumor cells and NIH/3T3 (mouse embryonic fibroblast cells) healthy cells by MTT assay (5). The chemical structures of the compounds were confirmed by IR, 1H NMR, 13C NMR and MS spectral data.

RESULTS:

The synthesized compounds indicated cytotoxic activity to different extends.

CONCLUSIONS:

This study increased the importance of bis(1,3,4-thiadiazole) compounds in the investigation of chemotherapeutic drugs.

REFERENCES:

1. Kaya B, Kaplancıklı ZA et al., (2017). Turkish Journal of Biochemistry, 42:131-137.
2. Abdelhamid AO, Gomha SM et al., (2018). Synthetic Communications, 48:677-684.
3. Gomha SM, Kheder NA et al., (2016). Molecules, 21:1532-1539.
4. Mohammadi-Farani A, Heidarian N et al., (2014). Iranian Journal of Pharmaceutical Research, 13:487-492.
5. Mossmann T (1983). Journal of Immunological Methods, 65:55-63.

P-499: SYNTHESIS OF NEW THIADIAZOLE DERIVATIVES AS ANTICANDIDAL AGENTS

[1] Kaplancikli, ZA., [1,2] Ozkay, Y. [1,2] Osmaniye, D., [1] Cavusoglu Kaya, B., [1,2] Acar Cevik, U., [1,2] Saglik, BN., [3] Ilgin, S., [4] Behcet, M., [1,2] Levent, S.

[1]Anadolu Universty, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskişehir, Turkey

[2]Anadolu Universty, Faculty of Pharmacy, Doping and Narcotic Compounds Analysis Laboratory, Eskişehir, Turkey

[3]Anadolu Universty, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Eskişehir, Turkey

[4]Abant İzzet Baysal Universty, Faculty of Medicine, Department of Medical Microbiology, Bolu, Turkey

INTRODUCTION:

Fungal infections have a continuous and serious threat to human health. The increased incidence of fungal infections is mainly due to an increase in the number of patients resistant to antifungal agents (1). It is obvious that azole derivatives represent a series of synthetic compounds of significant antifungal activity. The azoles show antifungal activity by inhibiting lanosterol 14α-demethylase. In other respects, it is well known that 1,3,4-thiadiazoles plays an important role for anticandidal activity (2,3). By virtue of the above consequence, in the present study novel 1,3,4-thiadiazole derivatives were synthesized to evaluate their antifungal activity.

MATERIALS AND METHODS:

The structures of the synthesized compounds were elucidated using FT-IR, 1H-NMR, 13C-NMR, and HRMS spectral data. Antimicrobial activity screening was performed according to EUCAST definitive method EDef 7.1 (4). Synthesized compounds were tested for their in vitro growth inhibitory activity against C. glabrata (ATCC 2001), C. parapsilosis (ATCC 22019), C. krusei (ATCC 6258), C. tropicalis (ATCC 13803), C. famata (Abant İzzet Baysal University Medical Faculty Hospital, clinic izolate), C. lusitaniae (Abant İzzet Baysal University Medical Faculty Hospital, clinic izolate) and C. albicans (ATCC 90028, ATCC 10231).

RESULTS:

Antimicrobial activity test revealed that the most active compound 3m (MIC=5 µg/ml) possesses 4 fold greater anticandidal effect than fluconazole (MIC=20 µg/ml) against C.albicans.

CONCLUSIONS:

It was observed that presence of 2,4-dichlorophenyl moiety enhances the anticandidal activity, significantly.

REFERENCES:

1. Irfan M, Aneja B et al., (2015). European Journal of Medicinal Chemistry, 93:246-254.
2. Salgin Goksen U, Gokhan Kelekci N et al., (2007). Bioorganic & Medicinal Chemistry, 15:5738-5751.
3. Levent S, Kaya Cavusoglu B et al., (2018). Molecules, doi:10.3390/molecules22112004
4. EUCAST.DefinitiveDocumentEDef7.1:Method-fortheDeterminationofBrothDilutionMICsofAnti-fungalAgentsforFermentativeYeasts..

P-500: SYNTHESES AND ANTIMICROBIAL ACTIVITIES OF NOVEL MONOCATIONIC INDOLE-BENZIMIDAZOLE DERIVATIVES

[1] Ates Alagoz, Z., [2] Yildiz, S., [1] Goker, H.

[1]Ankara University, Department of Pharmaceutical Chemistry, Ankara, Turkey

[2]Ankara University, Department of Microbiology, Ankara, Turkey

INTRODUCTION:

Syntheses of new benzimidazoles substitued at C-5 with several amidine derivatives were reported by us recently. These compounds showed a good activity profile as to Gram-positive bacteria and fungi. Compounds having bulky alkyl substituted at the N1-position of benzimidazole exhibited the greatest activity against S. aureus, MRSA, C. albicans and C. krusei of 0.78 - 1.56 µg/mL MIC values. In an attempt to find more active agents, we describe herein the synthesis of new analogues benzimidazoles substitued at C-5 with amidine and linked with indole ring at C-2 positions.

MATERIALS AND METHODS:

Several 1-substitue-2-(1H-indol-3-yl)-N-substitue-1H-benzimidazole-5-carboxamidine analogues were synthesized for their biological activities. Syntheses of new amidinobenzimidazoles were carried out starting from aromatic nucleophilic substitution of the chlorine atom of 4-chloro-3-nitrobenzonitrile with appropriated amines to provide the corresponding 3-nitro-4-substituted-aminobenzonitriles in good yields. The nitriles were converted to imidate esters with dry HCl gas in absolute ethanol and following reaction with various amines in ethanol gave the intermediate-

amidines. Reduction of nitro group with hydrogen gas by using palladium carbon and condensation of these derivatives with indole carboxaldehyde gave the targeted indole-benzimidazoles. Antimicrobial activity of all final compounds was evaluated in vitro against Gram positive bacteria S. aureus (ATCC 25923), Methicillin-resistant S. aureus (MRSA, ATCC 43300), and S. epidermidis (ATCC 12228).

RESULTS:

In this group, compound 11 showed the best result with a MIC value of 3.12 lg/mL against to MRSA, which is equal to Ampicilline. Also, compound 11 has activity against S. aureus, and S. epidermidis with 3.12 lg/mL, 6.25 lg/mL MIC values, respectively. Due to the labile hydrogen atom at the 3-position, the thiazolidine-2,4-dione was N-alkylated with appropriate phenacyl

CONCLUSIONS:

Future studies will include testing antimicrobial activities of the synthesized compounds against different bacteria and yeasts. In order to improve the antimicrobial activity, chemical synthesis of additional Novel Monocationic Indole-Benzimidazole derivatives are warranted.

REFERENCES:

1. Goker H, Kus C, Boykin DW, Yildiz S, Altanlar N (2002). Bioorg. Med. Chem., 10:2589–2596.
2. Ates Alagoz Z, Alp M, Kus C, Yildiz S, Buyukbingol E, Goker H (2006). Arch. Pharm. Chem. Life Sci., 339:74 – 80.

P-501: THE RECEPTOR TYROSINE KINASE INHIBITORY ACTIVITIES AND MOLECULAR DOCKING STUDIES OF SOME PYRROLO[2,3-D]PYRIMIDINE DERIVATIVES

[1] Kilic Kurt, Z., [2] Kurt, EE., [3] Bakar-Ates,F.

[1] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

[2] Yildirim Beyazit University, Faculty of Medicine, Department of Medical Genetics, Ankara, Turkey,

[3]Ankara University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey,

INTRODUCTION:

Receptor tyosine kinases (RTK) play a major role in signal transduction pathway that regulates critical cellular processes such as cell growth, proliferation, differentiation, migration and metabolism (1). Pyrrolo[2,3-d]pyrimidine are purine analogs that demonstrate a variety of biological activities such as antibacterial, antiviral, anticancer, anti-inflammatory, and antihyperglycemic activities (2). There are several pyrrolo[2,3-d]pyrimidine derivatives of RTK inhibitors such as AE788 and PKI166. In this paper, in vitro VEGFR-2, EGFR and PDGFR-β tyrosine kinase inhibitory activities of several pyrrolo[2,3-d] pyrimidines were evaluated. In addition, molecular docking studies of the active compounds with VEGFR-2, EGFR and PDGFR-β tyrosine kinases were carried out to speculate the possible binding mode of these molecules in the active site of target enzymes.

MATERIALS AND METHODS:

At present study, we evaluated the effects of test compounds on receptor tyrosine kinases such as VEGFR-2, EGFR ve PDGFR-β. The assays were performed using KDR Kinase Enzyme System Analysis Kit (Promega, #V2681), EGFR Kinase Enzyme System Analysis Kit (Promega, #V3831) and PDGFR-β Kinase Enzyme System Analysis Kits (Promega, #V3731) according to the manufacturer's instructions. The molecular docking studies were confirmed using Autodock vina program.

RESULTS:

Among the tested compounds, 9a, 9b and 11b exhibited the weak inhibitory activities against VEGFR-2, EGFR and PDGFR-β, respectively. Molecular docking studies showed that one or two hydrogen bonding interactions were found between compounds 9a, 9b, 11b and VEGFR-2, EGFR,PDGFR-β tyrosine kinases, respectively.

CONCLUSIONS:

All of the compounds exhibited poor inhibition on the tested RTKs. To obtain better activity results, it may be necessary to design some compounds showing more interaction with the target proteins

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (214S573)

REFERENCES:

1. Aveic S, Tonini GP. (2016). Cancer Cell. International, 16:62-70.
2. De Coen LM, Heugebaert TSA, García D. Stevens CV. (2016). Chemical Reviews, 116:80−139.
3. Hoekstra R, Dumez H, Eskens FA, Van Der Gaast A, et al. (2005). Clinical Cancer Research, 11:6908-6915.

P-502: THE ROLE OF GSTM1 AND GSTT1 POLYMORPHISMS IN OBESE PATIENTS

[1] Unsal, A., [1] Cihan, M., [1] Bulus, H., [2] Dirican, O., [2] Oguztuzun, S., [3] Ada, AO., [2] Gurbuz, N., [2] Kaygin, P., [3] Iscan, M.

[1]Kecioren Educational and Research Hospital, Department of Surgery, Ankara, Turkey

[2]Kirikkale University, Faculty of Arts and Sciences, Department of Biology, Kirikkale, Turkey

[3]Ankara University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

INTRODUCTION:

Obesity is a chronic disorder with increasing prevalence worldwide and occurs when energy intake is greater than energy expenditure. Oxidative stress is one of the factors that cause obesity and arises from an imbalance between the reactive oxygen species and cell's antioxidant defense system. Increasing ROS in obesity has an effect on the hypothalamic neurons which are involved in hunger and satiety control and consequently body weight control. On the other hand, weight loss due to calorie restriction or exercise reduces oxidative stress. Mitochondria is the most important source for ROS formation. In electron transfer system, reactive oxygen species forming as a result of oxidative phosphorylation reactions are involved in various physiological processes such as cell proliferation and differentiation. For the first time in our work, we investigated the role of GSTM1 and GSTT1 isoenzymes in obesity which has apoptosis mechanisms and cell cycle regulation in Turkish population.

MATERIALS AND METHODS:

In this study planned, in the light of this information, the role of GSTM1 and GSTT1 isoenzymes in 152 patients diagnosed with obesity was investigated.

RESULTS:

Findings have been shown to increase oxidative stress by GSTM1 and GSTT1 isoenzymes mutation in obese patients. There were no statistically significant associations between BMI, TSH, glucose, satiety blood glucose, triglyceride and cholesterol levels with GSTM1 and GSTT1 isoenzymes mutation in obesity patients.

CONCLUSIONS:

Our study supports the role of GSTM1 and GSTT1 isoenzymes, an important gene, in the development of obesity.

REFERENCES:

1. Role of Environmental Chemicals in Diabetes and Obesity: A National Toxicology Program Workshop Report. (2012). http://dx.doi.org/10.1289/ehp.1104597
2. Wright, SM, Aronne, LJ. (2012). Causes of obesity. Abdominal Imaging Journal, 37 (5), 730-2.
3. Codoñer-Franch P, Boix-García L, et al (2010). Is obesity associated with oxidative stress in children? International Journal of Pediatric Obesity, 5, 56–63
4. Vincent HK, Taylor AG. (2006). Biomarkers and potential mechanisms of obesity-induced oxidant stress in humans. International Journal of Obesity, 30, 400–418.
5. Hofbauer KG, Nicholson JR, et al. (2007). The obesity epidemic: current and future pharmacological treatments. Annual Review of Pharmacology and Toxicology, 47, 565-92.

P-503: INVESTIGATION OF GST ISOENZYMES AND APOPTOTOTIC EFFECT IN MCF7 HUMAN BREAST CANCER CELL LINE BEFORE AND AFTER DOXORUBICIN TREATMENT

[1] Oguztuzun, S., [2] Kocdogan, AK., [3] Simsek, GG., [1] Gurbuz, N., [4] Turk, M., [5] Isgor, Y., [6] Ada, AO., [6] Iscan, M.

[1]Kirikkale University, Faculty of Arts and Sciences, Department of Biology, Kirikkale, Turkey

[2]Istanbul Gelisim University, Vocational School of Health Sevices, Patology Laboratory Techniques, Istanbul, Turkey

[3]Kecioren Educational and Research Hospital, Department of Pathology, Ankara, Turkey

[4]Kirikkale University, Faculty of Engineering, Department of Bioengineering, Kirikkale, Turkey

5Ankara University Vocational School of Health Services Department of Pharmacy Services, Ankara, Turkey

6Ankara University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

INTRODUCTION:

Chemotherapy is widely administered for the treatment of breast cancer. However, despite its success, resistance to chemotherapeutic agents is a common occurrence that is often attributable to mechanisms of multidrug resistance (MDR) (1). Chemoresistance is a multifactorial phenomenon and many studies clearly show that a coordinated expression of efflux transporter proteins and glutathione S-transferases (GSTs) in tumor cells is linked to the development of the multidrug resistance phenotype (2, 3). GST

is known to mediate biotransformation of various anticancer drugs and its elevated has been reported in various resistant cancer cell lines like MCF-7. In particular, the overexpression of glutathione S-transferases and efflux pumps in tumors may reduce the reactivity of various anticancer drugs. p38, bcl-2 and caspase-3 have a role in apoptosis (4, 5). In this study, immunocytochemical expressions of GST Alpha-1 (GSTA-1), GST Mu-1 (GSTM1), GST Theta-1 (GSTT1), GST Pi-1 (GSTP1), GST Omega-1 (GSTO1), GST Zeta-1 (GSTZ1), GST Sigma-1 (GSTS1), GST Kappa-1 (GSTK1), p38, bcl-2 and caspase-3 were examined in MCF7 human breast cancer cell line before and after Doxorubicin treatment.

MATERIALS AND METHODS:

Doxorubicin was added at a concentration of 0, 1, 2,5 or 5 µM and cells were continuously treated at 37°C and 5% CO2 for 10–12 days for colony formation. After incubation, colonies were washed in PBS, fixed with methanol for 15 min and washed in PBS. The harvested breast cells were immunostained.

RESULTS:

Treated and untreated cancer cells were scored according to their immunostaining intensity. The GSTP1, GSTT1, GSTM1, GSTA1, GSTO1, GSTZ1 and GSTK1 expressions were higher in treated breast cancer cells than those in untreated doxorubicin human breast cancer cells. Similarly, the p38, bcl-2 and caspase-3 expressions were higher in treated breast cancer cells than that in untreated doxorubicin human breast cancer cells. However, there was no statistical difference in GSTS1 expression.

CONCLUSIONS:

In conclusion, elevated expressions of GSTP1, GSTT1, GSTM1, GSTA1, GSTO1, GSTZ1, GSTK1, p38, bcl-2, p53 and caspase-3 might be important in doxorubicin resistance in breast cancer.

ACKNOWLEDGEMENTS:

This study was supported by a grant of Kırıkkale University BAP(2014/32)

REFERENCES:

1. Huang J, Tan PH, et al., (2003). Mod Pathol 16(6):558–565.
2. Nakanishi Y, Kawasaki M, et al., (1999). Oncology 57: 318–23.
3. Oguztuzun S, Iscan M, et al., (2009). Turkish Journal of Biology, 33: 89-100.
4. Gottesman MM (2009). Methods in Molecular Biology, 596: 47-76.
5. Saua A, Pellizzari Tregnoa F, et al., (2010). Archives of Biochemistry and Biophysics 500 (2): 116–122.

P-504: HEALTH RISK ASSESSMENT OF CHILDREN PLAYGROUNDS IN SARAJEVO

[1] Sapcanin, A., [1] Smajovic, A., [1] Salihovic, M., [2] Uzunovic, A., [1] Spirtovic Halilovic, S., [3] Pehlic, E., [4] Jancan, G.

[1]University of Sarajevo,Faculty of Pharmacy, Sarajevo, Bosnia and Herzegovina,

[2]Agency for Medicinal Products and Medical Devices, Sarajevo, Bosnia and Herzegovina,

[3]University of Bihac, Faculty of Biotechnical Sciences, Bihac, Bosnia and Herzegovina,

[4]Chemilab d.o.o., Ljubljana, Slovenia.

INTRODUCTION:

Risk assessment is a multi step procedure that comprises data collection, exposure assessment, toxicity assessment and risk characterisation. Due to the children's low tolerance to pollutants, the health risk is very high for children's population. The aim of this study was to estimate the risk posed to children's health based on the content of heavy metals found in the soils of the children's playgrounds in Sarajevo urban area.Cd, Pb, Cr, Ni, Cu, Zn, Co, Fe, Se and As were identified as potential hazardous agents in soils at playgrounds.

MATERIAL AND METHODS:

Analysis of contamination of soil samples has been carried out, with soil samples having been taken from selected children's playgrounds which are situated close to potential polluters in the area of Sarajevo city. In order to asses the health risk posed to children and adults, the content of heavy metals, namely of Cd, Pb, Cr, Ni, Cu, Zn, Co, Fe, As, has been measured and the hazard coefficient (HQ) and non-cancerogenic hazard index (HI) have been calculated.

RESULTS:

The results have shown that the soil in the children's public playgrounds in Sarajevo city can be identified as mildly to excessively contaminated, and mildly to moderately soiled with heavy metals. Calculations have shown that values obtained for HQ and HI in children's playgrounds are lower than the standard values equal to 1, so that they do not pose risk for adults. The highest values of HI are obtained if taken orally, and the lowest if inhaled. The highest values of HI are obtained for Cr.

CONCLUSIONS:

In conclusion, public children's playgrounds in Sarajevo can be regarded as areas of high risk for children's health and children represent the highest portion of visitors to such places. Generally speaking, the soil contaminated with heavy metals can be used as a diagnostic tool to assess health risks posed to children and adults.

ACKNOWLEDGEMENTS:

This work was supported by the Federal Ministry of Education and Science in Bosnia and Herzegovina and was carried out within the framework of the project „Assessment of health risk caused by heavy metal contamination of the soil in the children's playgrounds in Sarajevo" (Grant no. 0101-7552-17/15, dated 14.12.2016).

REFERENCES:

1. De Miguel E, Iribarren I, et al., (2007). Risk-based evaluation of the exposure of children to trace elements in playgrounds in Madrid (Spain). Chemosphere , 66(3): 505−13.
2. Shi G, Chen Z, et al., (2011). A comparative study of health risk of potentially toxic metals in urban and suburban road dust in the most populated city of China. Atmos Environ , 45(3): 764−71.
3. Acosta JA, Cano AF, et al., (2009). Distribution of metals in soil particle size fractions and its implication to risk assessment of playground in Murcia City (Spain). Geoderma , 149(1−2): 101−9.

P-505: IN VITRO GENOTOXICITY AND CLASTOGENICITY EVALUATION OF CARBON-BASED ENGINEERED NANOPARTICLES (CDS)

[1] Sukuroglu, AA., [2] Simsek, S., [3] Yetkin, D., [2] Ozbek, B., [3,5,6] Battal, D., [3,4] Genc, R.

[1] Gazi University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Ankara, Turkey

[2] Yildiz Technical University, Department of Chemical Engineering, İstanbul

[3] Mersin University, Advanced Technology Research and Application Center, Mersin, Turkey

[4] Mersin University, Faculty of Engineering, Department of Chemical Engineering, Mersin, Turkey

[5] Mersin University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Mersin, Turkey

6Near East University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Nicosia, Cyprus

INTRODUCTION:

Fluorescence carbon nanoparticles (CNPs or C-dots, CDs) are often used in bio-imaging, sensor applications, and photocatalytic processes etc.. Moreover, due to their small size, they also have been investigated for their potential as multifunctional vehicles for drug delivery, with a specific focus on drug delivery to the nucleus (1-4). This opens the questions on the requirement of genotoxicity studies combined with cytotoxicity assessments.

Material and methods: In this study, in vitro genotoxicity and clastogenicity of carbon dots synthesized from both ethanolic (C-DotE@PEG) and aqueous(C-DotW@PEG) extract of Nerium oleander were performed on human breast cancer cell lines (MCF-7). Three different C-dots concentrations (0.25, 2.5 and 50 ppm) were evaluated via comet assay (Single Cell Gel Electrophoresis, (SCGE)) and cytokinesis-block micronucleus test (CBMN) methods in a time range of 72 h. In this study, in vitro cytokinesis-block micronucleus testing of nanomaterials was based on the draft OECD guideline (OECD TG 487) (5).

RESULTS:

As a summary, although cytotoxicity findings showed that C-dots were synthesized from aqueous (C-DotW@PEG) and ethanolic (C-DotE@PEG) extracts of Nerium oleander were not dramatically toxic on MCF-7 cells they showed different levels of genotoxicty and clastogenicity over the cells due to time and concentration.

CONCLUSIONS:

Further studies are warranted to evaluate the toxicity of C-dots depending on particle size and surface properties along with investigating the mutagenicity or carcinogenicity of C-DotE@PEG and C-DotW@PEG on mammalian cells for offering certain cautions and assessing their risks on humans.

REFERENCES:

1. Cha C, Shin SR, et al., (2013). Khademhosseini, Carbon-based nanomaterials: Multifunctional materials for biomedical engineering, ACS Nano. 7:2891–2897. doi:10.1021/nn401196a.
2. Chawla J, Kumar A (2013). Ranking Carbon-based Nanomaterials using Cytotoxicity to Minimize Public Health Risks, 4:301–308.
3. Chen C, Haifang W (2016). Biomedical Applications and Toxicology of Carbon Nanomaterials, doi:10.1002/9783527692866.
4. OECD guidelines for the testing of chemicals,(2010). Test No.487: In vitro Mammalian Cell Micronucleus Test. 487:23 http://dx.doi.org/10.1787/9789264091016-en.

P-506: EFFECTS OF PRENATAL BISPHENOL A AND/OR DI(2-ETHYLHEXYL) PHTHALATE EXPOSURE ON TESTICULAR OXIDATIVE STRESS AND SPERM PARAMETERS

[1] Balci, A., [1,2] Ozkemahli, G., [1] Erkekoglu, P., [3] Zeybek, ND., [3] Yersal, N. [1,4] Kocer Gumusel, B.

[1]Hacettepe University, Faculty of Pharmacy, Department of Toxicology, 06[1]00 Ankara, Turkey;

[2]Erzincan University, Faculty of Pharmacy, Department of Toxicology, Erzincan, Turkey;

[3] Hacettepe University, Faculty of Medicine, Department of Histology and Embryology, Ankara, Turkey

[4]Lokman Hekim University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

INTRODUCTION:

Bisphenol A (BPA) and di (2-ethylhexyl) phthalate (DEHP) are endocrine disruptor chemicals which are used in a wide variety of industrial products (1). Exposure to these substances is increasing due to their abundant use in daily life (1). Prenatal and early postnatal exposures is more critical and can lead to serious toxic effects like reproductive problems and hormonal disturbances (1). The aim of this study was to evaluate the prenatal and early postnatal (lactation) effects of BPA and/or DEHP exposure on sperm parameters and testicular oxidative stress in rats.

MATERIALS AND METHODS:

Pregnant Sprague-Dawley rats were divided randomly to four groups (n=3/group). Control group, DEHP group (30 mg/kg/day), BPA group (50 mg/kg/day) and DEHP-BPA group (30 mg/kg/day DEHP and 50 mg/kg/day BPA) were exposed through 6-21 gestational days and lactation period by intra-gastric lavage. Male offspring (n=6/group) from each mother were fed until the end of twelfth postnatal week, were then euthanized and sperm parameters (count, motility and morphology) were readily determined. Oxidative stress parameters (lipid peroxidation, protein oxidation, glutathione levels, and oxidative DNA damage) were investigated in testicular tissue homogenates.

RESULTS:

Both sperm counts and motilities were significantly lower in all of the study groups vs. control ($p<0,05$). Normal sperm morphology was also markedly lower in all of the study groups vs. control (91% in control, 72% in DEHP group, 61% in BPA group and 42% in DEHP+BPA group) ($p<0,05$). Total glutathione levels were significantly decreased in BPA, DEHP and BPA+DEHP groups versus control (31%, 27% and 26%, respectively). Lipid peroxidation (MDA) levels were higher in DEHP and DEHP+BPA groups versus control (%28 and %60, respectively; $p <0,05$, both). These results show that early-life exposure to EDCs can cause significant unwanted effects on sperm parameters and can lead to oxidative stress in testis tissues of rats.

CONCLUSIONS:

Deterioration in sperm parameters indicate that both single and combined exposures to BPA and DEHP may reduce fertility in rats. Combined exposure to BPA and DEHP particularly caused more significant effects on sperm parameters and testicular oxidative stress parameters. In BPA plus DEHP group, decreases in total glutathione levels and increases in lipid peroxidation suggest that oxidative stress may be one of the possible underlying mechanisms for the combined adverse effects of these chemicals. More studies are needed to show the reprotoxic effects of combined exposure to EDCs in biological systems.

ACKNOWLEDGEMENTS:

This study was supported by Hacettepe University Scientific Projects Coordination Unit.

REFERENCES:

1. Diamanti Kandarakis E, Bourguignon JP, et al., (2009). Endocrine-disrupting chemicals: an Endocrine Society scientific statement. Endocrine Reviews, 30(4):293-342.

P-507: EVALUATION OF CYTOTOXIC AND GENOTOXIC EFFECTS OF BORIC ACID AND ZINC BORATE ON HUMAN SERTOLI CELLS

Ustundag, A., Eroglu, M., Duydu, Y.

Ankara University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

INTRODUCTION:

Boric acid and zinc borate are among the most important exportation products of Turkey. Zinc borate is typically composed of 45% ZnO and 34% boric anhydride (B2O3), with 20% water of hydration. Zinc borate readily breaks down in the stomach to zinc oxide and boric acid. Boron compounds have been considered as being toxic to reproduction system in animal experiments. In addition, reproductive data of boron exposure is very limited. Because of the limited information in the literature on the toxicity of zinc borate, this study is substantial as we use the reproductive system cell which is the target of boron exposure. The aim of our study is to investigate the cytotoxic and genotoxic effects of boric acid and zinc borate on Sertoli cell culture in vitro. These data will contribute our previous studies and support the health and environmental authorities for preparation of the legal regulation about boron compouds.

MATERIALS AND METHODS:

The cytotoxicity of boric acid and zinc borate was determined by using Neutral Red Uptake (NRU) assay. Comet assay was performed to investigate the DNA integrity of boric acid and zinc borate in different

concentrations. Muse Annexin V& Dead Cell Kit was used to determine apoptosis Muse Oxidative Stress Kit was used to determine Reactive Oxygen Species (ROS) by using Muse Cell Analyser on Sertoli cell culture.

RESULTS:

Acording to our results, boric acid has no cytotoxic effect and does not induce apoptosis up to 1000 µM. In addition, boric acid does not induce comet tail intensities and ROS up to 500 µM on human Sertoli cells. Besides, zinc borate is cytotoxic on human Sertoli cells (IC50=90µM) and significantly induces apoptosis at 100 µM. In addition, zinc borate is significantly induces comet tail intensities and reactive oxygen species at 50 µM on human Sertoli cells.

CONCLUSIONS:

The results of our study demonstrates that zinc borate causes oxidative stress, induces cell death and apoptosis and DNA strand breaks at relatively high concentrations.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-115S983)

REFERENCES:

1. Duydu Y, et al., (2012). Archives of Toxicology, 86, 27-35.
2. Duydu Y, et al., (2012). Journal of Trace Elements in Medicine and Biology, 26, 161-164.
3. Celikezen FC, et al., (2014). Toxicological & Environmental Chemistry, 96, 777-782
4. Turkez H, et al., (2010). Acta Biochimica Polonica, 57(1), 95-7.

P-508: INVESTIGATION OF IRRITATION EFFECTS OF SUNSCREEN FORMULATIONS CONTAINING TIO2 NANOPARTICLES BY USING THE EPIDEM SKIN IRRITATION TEST

[1] Ulker, OC., [2] Teker, E.,[1] Ustundag, A., [3] Sezgin Bayindir, Z., [1] Duydu, Y., [1] Karakaya, A.

[1]Ankara University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

[2] Biomerieux Diagnostics, Clinical Marketing Department, Istanbul, Turkey

[3] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara Turkey

INTRODUCTION:

Metal oxide nanoparticles (NP) such as titanium dioxide have been used increasingly in various cosmetics especially sunscreens. Because of widespread environmental exposure to metal oxide nanoparticles, it is urgent to elucidate their effects on human health. Recently, various toxic effects of TiO2 NPs have been investigated in cell lines using different endpoints. The EpiDerm Skin Irritation Test is a validated in vitro method for investigating the skin irritation potency of the ingredients of the cosmetics and finished cosmetic products as well. The aim of this study was to investigate the irritation effects of sunscreen formulations containing two different nanosize and two different concentrations of TiO2 NPs by EpiDerm Skin Irritation Test.

MATERIALS AND METHODS:

The sunscreen formulation samples that contained two different particle size and two different concentration of TiO2 NPs were prepared as oil-in-water (o/w) emulsions. The concentrations were selected as 5% and 10% by considering the TiO2 NPs contained sunscreen formulations in the market. Irritation potency of the samples were detected by EpiDerm Skin Irritation Test. The irritant chemicals have abilities to penetrate stratum corneum, after penetration they are cytotoxic to the cells in the below layers. Therefore the princible of the multilayer 3D EpiDerm Skin Irritation Test procedure based on the MTT cytotoxicity assay. Sodium Dodecyl Sulphate (SDS) in 5% concentration and Dulbecco's Phosphate Buffer Solution (DPBS) were used as positive and negative controls, respectivly. The optical density (OD) values obtained with each sample were used to calculate the percentage of viability compared with the negative control that is set at 100%.

RESULTS:

Exposure to sunscreen formulation that contained 20 nm 10% TiO2 resulted in significantly decreased cell viability in EpiDerm Skin Irritation Test. According to our results it might be suggested that %5 TiO2 NPs contained sunscreen products can considered safe. However sunscreen products containing small naoparticles and high concentration of TiO2 NP may cause skin irritation.

CONCLUSIONS:

Our results are shown a valuable and original information on the skin irritation potency of TiO2 NPs contained sunscreen products.

ACKNOWLEDGEMENTS:

This study was supported by a grant of TUBITAK (SBAG-113S229)

REFERENCES:

1. Buzea C, Pacheco I, et al., (2007). Biointerphases 2:17-70.
2. Botelho MC, et al., (2014). Biomed Pharmacother 68:59-64.
3. European Commision (2013). EURL ECVAM progress report on the develeopment, validation and regulatory acceptance of alternative methods.

P-509: PROTECTIVE EFFECTS OF CHLOROGENIC ACID AND VITAMIN C AGAINST OXIDATIVE STRESS CAUSED BY DIMETHOATE IN HUMAN ERYTHROCYTES

Eken, A., Bakir, E., Okcesiz, A.

Erciyes University, Department of Pharmaceutical Toxicology, Kayseri, Turkey

INTRODUCTION:

Dimethoate is one of the most important organophosphate insecticides that has been shown to induce oxidative stress through the generation of free radicals and alteration of the cellular antioxidant defense system. The aim of the study was to assess the protective effects of chlorogenic acid and vitamin C as an antioxidant compounds on dimethoate-induced oxidative stress in human erythrocytes in vitro.

MATERIALS AND METHODS:

Human fresh blood were collected in tubes from three healthy female volunteers by venipuncture. Heparin was used as an anticoagulant. Erythrocytes were separated from blood plasma by centrifugation (4400 rpm for 10 min at 4°C) and then washed three times with a cold isotonic saline solution (0.9% NaCl). The supernatant and the buffy coat were carefully removed after each wash. After separation, erythrocytes were suspended in phosphate buffer saline (PBS) pH 7.4 and used for different incubations. Erythrocytes were divided into portions. The first portion was incubated for 4 h at 37°C with different doses (10, 35, 70 mM) of dimethoate. The other portions were preincubated with chlorogenic acid (20 mM) and vitamin C (1 mM) for 30 min, followed incubation with dimethoate for 4 h at 37°C. Malondialdehyde (MDA) concentrations as a lipid peroxidation index and antioxidant enzyme activitiy of catalase (CAT) were measured in all treatment portions of erythrocytes. Erythrocyte morphology were evaluated by light microscopy at 40x magnification.

RESULTS:

Treatment with dimethoate alone increased the level of MDA and activitiy of CAT in erythrocytes as compared with nontreated control cells ($P<0.05$). Treatment of cells with chlorogenic acid + dimethoate or vitamin C + dimethoate prevented dimethoate-induced changes in antioxidant enzyme activity and lipid peroxidation. However, this effect was seen only at low concentration of dimethoate (10 mM). In addition, deleterious morphological changes in erythrocyte were also observed in the presence of dimethoate.

CONCLUSIONS:

These results suggest that chlorogenic acid or vitamin C may play a role in reducing dimethoate-induced oxidative stress in human erythrocytes in vitro.

P-510: EVALUATION OF CD33 LEVELS IN ALZHEIMER'S DISEASE: A PRELIMINARY STUDY

[1] Perk, BO., [2] Ozkan, T., [1] Guven, NM., [2] Sunguroglu, A., [1] Eke, BC.

[1] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Ankara, Turkey

[2]Ankara University, Faculty of Medicine, Department of Medical Biology, Ankara, Turkey

INTRODUCTION:

Alzheimer's disease (AD) which is a chronic, complex and multifactorial neurodegenerative disorder is the most common cause of progressive cognitive and functional decline in the elderly. Many genes have been identified as AD risk factors and CD33 is a new genetic risk factor associated with AD. CD33 which is a type I transmembrane protein is involving in immune regulation. CD33 expression has been shown to be increased in microglia cells in the Alzheimer brain and has a positive correlation with the severity of the disease. Additionally, it is demonstrated that CD33 levels are down-regulated in peripheral blood mononuclear cells (PBMCs) of AD subjects. In this preliminary study, blood CD33 levels were compared with AD patients and normal controls over 65 years of age [1,2].

MATERIALS AND METHODS:

Our preliminary study was comprised of 6 AD patient (mean age = 79.5 ± 7.3 years) and 12 cognitively normal controls (mean age = 80.83 ± 5.6 years) matched for sex and age. Samples of peripheral blood were collected into tubes containing EDTA, from each of the 6 AD patients and 12 controls. PBMCs from 10 ml of the peripheral blood with EDTA were obtained by density gradient centrifugation with lymphoprep and then washed in phosphate buffer phosphate saline. CD33 protein levels were examined using BD Accuri™ C6 flow cytometer with FITC anti-human CD45, PE anti-human CD33, PE Mouse IgG1 κ Isotype Ctrl and FITC Mouse IgG1 κ Isotype Ctrl (BIOLEGEND). All experimental data were expressed as mean ± standard deviation (SD).

RESULTS:

We found that the percentage of CD33 positive monocytes was lower in AD group than control (7.63 ± 1.81% versus 11.47 ± 2.00%).

CONCLUSIONS:

The results obtained in this study need further investigations in order to clarify CD33 level and AD.

ACKNOWLEDGEMENTS:

This study is supported by AUBAP (Project no: 17L0237008).

REFERENCES:

1. Hu N, Tan MS, Sun, et al., (2014). Decreased expression of CD33 in peripheral mononuclear cells of Alzheimer's disease patients, Neuroscience Letters, 563:51–54.
2. Griciuc A, Serrano-Pozo A, et al., (2013). Alzheimer's Disease Risk Gene Cd33 Inhibits Microglial Uptake Of Amyloid Beta, Neuron, 78(4): 631-643.

P-511: GENOTYPING RS2414096 VARIANT OF CYP19A1 GENE IN TURKISH POPULATION

[1] Altun, B., [1] Kadioglu, E., [1] Ipek, C., [2] Doger, E., [2] Bideci, A., [1] Attaran, H., [1] Cok, I.

1Gazi University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Ankara, Turkey

2Gazi University, Faculty of Medicine, Department of Pediatric Endocrinology, Ankara, Turkey

INTRODUCTION:

Genetic variations in human genome have long been studied to understand how genetic variation influences the risk of diseases. In this perspective, population based-genetic association studies represents us a unique opportunity to understand the genetic underpinnings of complex diseases for a given population. CYP19A1 is a polymorphic gene that encodes aromatase enzyme which catalyzes the last step of estrogen biosynthesis converting androgens to estrogens. Recently, rs2414096 SNP (A/G) in CYP19 gene have been associated with several endocrinologic diseases such as hyperandrogenism, male infertility and polychistic ovary syndrome (1,2). In this study, we aimed to determine the genotype and allele frequencies of rs2414096 variant of CYP19 gene in Turkish population.

MATERIALS AND METHODS:

182 unrelated healthy Turkish volunteers (109 females and 73 males, aged 12-80) recruited the study. Other ethnic groups were excluded. Blood samples were taken into the blood collection tubes (EDTAK2) and genomic DNA was extracted from whole blood by using High Pure PCR Template Preparation Kit (Roche, Germany). Genotyping of rs2414096 was performed with the RT-PCR method by using LightSNiP assay (TibMolbiol, Germany).

RESULTS:

The frequencies of AA, AG and GG genotypes were found 15.4%, 46.7% and 37.9%, respectively. Genotype distributions were in Hardy–Weinberg Equilibrium ($p>0.05$). The mutant allele (A) frequency was 0.38, compatible with the genomic databases (3).

CONCLUSIONS:

In conclusion, this study will contribute the understanding of biological basis of genetic susceptibility to several diseases in Turkish population. In the future, verifying genetic markers through case-control studies in Turkish population is needed to analyze potential genetic factors which contribute to etiology of complex diseases such as polycystic ovary syndrome.

ACKNOWLEDGEMENTS:

Special thanks to Dr. Erdem ŞAHİN, M.D from Emergency Service of Ankara Training and Research Hospital for his contribution to this study.

REFERENCES:

1. Jin JL., Sun J, et al., (2009). Association between CYP19 gene SNP rs2414096 polymorphism and polycystic ovary syndrome in Chinese women. BMC medical genetics, 10(1), 139.
2. Faizullin LZ, Kh TO, et al., (2013). Role of aromatase gene (CYP 19) polymorphism in the development of infertility in obese males. Obstetrics and Gynecology, 10, 76-80.
3. NCBI-dbSNP: 2414096
4. https://www.ncbi.nlm.nih.gov/projects/SNP/snp_ref.cgi?rs=2414096 (11.04.2018, accessed)

P-512: TERATOGENICITY AND TESTIS TOXICITY IN OFFSPRING OF PREGNANT RATS EXPOSED LEVETIRACETAM

[1] Kaya, C., [2] Cavusoglu, I., [1] Uzun, F., [2] Kadioglu, M., [1] Kerimoglu, G., [1] Yenilmez, E.

[1]Karadeniz Technical University, Faculty of Medicine, Department of Histology and Embriology, Trabzon

[2] Karadeniz Technical University, Faculty of Medicine, Department of Pharmacology, Trabzon

INTRODUCTION:

The current rate of the use of antiepileptic drugs in pregnancies is 0.3-0.4% (1,2). Exposure to a teratogenic substance during organogenesis period affects fetal development and functions of the organs. During this period, structural damage can occur which can not be repaired because the tissues are capable of rapid differentiation. In animal experiments, Levetiracetam (LEV) has been reported to transport the fetus directly through the placenta. Although there are limited informations on the teratogenic effect of LEV, there is no adequate information about testicular toxicity (2,3).

MATERIALS AND METHODS:

15 adult Spraque Dawley female rats (the weight range; 200-250 g) were left to mate with male rats. These 15 healthy pregnant rats were divided into 5 groups. No treatment was administered to the control group. Levetiracetam (100 mg / kg = 1 ml)

was administered to the LEV-A group (1st trimester, 0-7th day), LEV-B group (2nd trimester, 8-14th day), LEV-C group (3rd trimester, 15-21th day) and LEV-D group (throughout the pregnancy) by oral gavage. Testicular specimens were removed from offsprings. The fibrotic connective tissue formed during testicular development was evaluated morphometrically. Skull and extremity specimens were removed from pups. The samples prepared with haematoxylin-eosin staining were evaluated with a light microscope.

RESULTS:

Eyelid malformation was observed in the skull specimens of the LEV-D group while no malformation was found in the pups of the LEV-A, LEV-B and LEV-C groups, Cleavages (palate deformities) between the oral cavity and the nasal cavity was observed in the skull specimens of some of the LEV-D group rats. Significant increase was observed in the areas of testicular fibrotic connective tissue indicating testicular toxicity in the LEV-C and LEV-D groups when compared to the control group ($p<0.05$, $p>0.05$).

CONCLUSIONS:

The data revealed that levetiracetam exposure in the third trimester and throughout the pregnancy may cause testicular toxicity in offsprings. Additionally, LEV may cause possible mild teratogenic effects. Further studies are needed to confirm the testis toxicity and teratogenicity effects of LEV in the pregnancy.

ACKNOWLEDGEMENTS:

This study was supported by a grant of BAP (TYL-2017-5738)

REFERENCES:

1. Richmond JR, Krishnamoorthy P, et al., (2004). Epilepsy and pregnancy : An obstetric perspective. Am J Obstet and Gynecol 2004; 190: 371.
2. Kayaalp S, et al., Rasyonel Tedavi Yönünden Tıbbi Farmakoloji. Hacettepe Taş Kitapçılık Limited Sti., 2005.
3. Hill, Denise S, et al., “Teratogenic effects of antiepileptic drugs.” Expert review of neurotherapeutics 10.6 (2010): 943-959.

P-513: QUANTITATIVE DETERMINATION OF URINARY DOPAMINE BY A HIGHLY SENSITIVE LC-MS/MS ASSAY

[1,2] Battal, D., [3] Aktas Sukuroglu, A., [2] Alkas, FB.,[4] Unlusayin, I.

[1]Mersin University, Department of Toxicology, Mersin, Turkey.

[2]Near East University, Department of Toxicology, Nicosia, Cyprus

[3] Gazi University, Department of.Toxicology, Ankara, Turkey

[4] Acıbadem Labmed, İstanbul, Turkey.

INTRODUCTION:

Dopamine (DA) is a prominent neurotransmitter. Depending on the postsynaptic receptor, it produces either excitatory and inhibitory postsynaptic potentials. In the central nervous system (CNS), DA is involved in the control of mood, movement, cognition, motivation and reward pathways. In the peripheral nervous system (PNS), it controls Na+ homeostasis in kidney, renal blood flow and cardiovascular functions. Additionally, it is a hypothalamic neurohormone regulating prolactin release from the anterior pituitary, and recent evidence suggests that it has immunoregulatory functions. The determination of DA facilitates better understanding of the complex brain disorders in the central nervous system and the regulation of endocrine system, cardiovascular functions and renal functions in the periphery (1, 2). The purpose of this study was to develop a highly sensitive and reliable assay for the quantification of DA in urine using liquid chromatography-tandem mass spectrometry (LC-MS/MS).

MATERIALS AND METHODS:

The aim of the present study was to develop a rapid, sensitive and simple LC-MS/MS method for the simultaneous and quantitative analysis of dopamine levels in urine. The LC-MS/MS separation was performed on a Zorbax SB-C18 3.0 x 50 mm 3.5 micron 600 BAL with a gradient elution system of formic acid-water as the mobile phase.

RESULTS:

A rapid, sensitive and robust method was developed, validated and used for the trace analysis of dopamine in urine by LC-MS/MS. The method was validated in artificial urine samples following the guidelines of the European Medicines Agency in terms of selectivity, linearity, calibration range, limit of detection (LOD), limit of quantitation (LOQ), carryover, accuracy, precision, dilution integrity, matrix effect, robustness, and stability, obtaining adequate results in all parameters. The linear ranges for dopamine were 20 - 2000 ng/mL. The correlation coefficient was greater than 0.998. The LOD and LOQ for dopamine were 0.36 and 1.215 ng/mL, respectively. The recoveries were 95.622 - 101.200 with RSD<5%.

CONCLUSIONS:

The required functional sensitivity was achieved by this method, quantitating analytes over a sufficiently wide dynamic range. It will be also demonstrated that precise quantification of dopamine concentration levels in urine yield better understanding of the pathophysiology and pathogenesis of neuropsychiatric disorders and of research for new drugs. This new LC-MS/MS-based method significantly simplifies the detection procedure for DA in urine.

REFERENCES:

1. Kamila Syslová, Lukáš Rambousek et al. (2013). In: Dopamine : Functions, Regulation and Health Effects (ed). Dopamine Analysis in Neuroscience Research. Nova Science Publisher, United States of America, pp 81-112.
2. Ferrer DG, García AG, Peris-Vicente J, Gimeno-Adelantado JV, Esteve-Romero J (2015). Anal Bioanal Chem 407: 9009.

P-514: CYTOTOXIC AND GENOTOXİC EFFECTS OF FLURBİPROFEN IN HELA CELLS

[1] Bakir, E., [2] Aydin, S., [1] Eken, A., [2] Undeger Bucurgat, U.

[1] Erciyes University, Department of Pharmaceutical Toxicology, Kayseri, Turkey

[2] Hacettepe University, Department of Pharmaceutical Toxicology, Ankara, Turkey

INTRODUCTION:

Protective effects of nonsteroidal anti-inflammatory drugs (NSAIDs) against cancer and anticancer effects have become a remarkable topic. In vitro, in vivo, and epidemiological studies have all demonstrated that NSAIDs appear to be effective in the chemoprevention and possible treatment of many cancers including colorectal, breast, prostate, pancreatic, squamous cell carcinoma of the head and neck, ovarian, lung, and bladder cancers (1). In this study, our aim was to assess cytotoxic and genotoxic effects of “flurbiprofen”, a propionic acid derived NSAI, in the human cervical cancer cell (HeLa).

MATERIALS AND METHODS:

Cytotoxicity of flurbiprofen in HeLa cells was measured by using Thiazolyl Blue Tetrazolium Blue (MTT) assay for 24 h, 48 h, 72 h and at dose range of 5-3000 μM, and genotoxicity was evaluated by using alkaline comet assay at doses determined according to cytotoxicity results/pharmacokinetic properties of drug, non-cytotoxic doses for 48 h. DNA damage was expressed as tail length, tail intensity, and tail moment.

RESULTS:

The IC50 doses of flurbiprofen in HeLa cells were found to be 2594 μM, 990 μM, and 907 μM according to exposure times, respectively and cytotoxicity was increased by dose-dependent. DNA damage was observed in HeLa cells exposed to flurbiprofen for 48 h at the indicated doses and statistically significant manner compared to the negative control ($p<0.05$). This DNA damage was also increased by dose-depended.

CONCLUSIONS:

According to the results of our study; flurbiprofen have been cytotoxic effect by dose-depended manner and caused DNA damage in the HeLa cell line at low non-cytotoxic doses. Therefore, it is thought that it may contribute to antitumor effect against cervical cancer. Otherwise, since there isn’t enough data on the mutagenicity of flurbiprofen, our study will contribute to the literature.

ACKNOWLEDGEMENTS:

The part of this study was supported by Research Fund of the Erciyes University Scientific Research Project Unit (Project number: TDK-2017-7376).

REFERENCES:

1. Andrews P, et al., (2008). ‘A comparison of the effectiveness of selected non-steroidal anti-inflammatory drugs and their derivatives against cancer cells in vitro’, Cancer Chemotherapy and Pharmacology, 61:203-214.

P-515: ADSORPTION CHARACTERISTICS OF ISONIAZID ON GRAPHENE OXIDE

[1] Caliskan Salihi, E., [1] Kirkulak, S., [2] Wang, J., [2] Siller, L.

[1]Marmara University, Faculty of Pharmacy, Department of Basic Pharmaceutical Sciences, Istanbul, Turkey

[2]Newcastle University, School of Chemical Engineering and Advanced Materials, United Kingdom

INTRODUCTION:

One of the growing environmental problems is the presence of drugs in the environment. Especially, the presence of antibiotic residues in waters leads to a variety of adverse effects, such as chronic toxicity and microorganism antibiotic resistance. The adsorption method becomes an effective and attractive alternative for the treatment of waters containing drug residues. Because the adsorption method is economical, flexible in design, easy to operate and insensitive to toxic pollutants (1). Recent studies showed that graphene based materials can be used as adsorbents for water treatment (2). So the aim of the present study is to investigate the adsorption characteristics of isoniazid on graphene oxide.

MATERIALS AND METHODS:

Graphene oxide was produced using Hummers method revised in our laboratory (2). Adsorption experiments were done as a function of time, initial concentrations, graphene oxide amount and pH.

RESULTS:

Results of the experiments showed that the adsorption process reached the equilibrium in 1 hour and it occurs according to L-type of the Giles classification.

CONCLUSIONS:

Adsorption characteristics of isoniazid on graphene oxide was studied at various experimental conditions. Graphene oxide was capable of being an adsorbent for the adsorption of the selected antibiotic molecule, isoniazid. The main driving force of the adsorption of isoniazid on graphene oxide was electrostatic attraction with the contribution of π-π dispersion interactions.

REFERENCES:

1. Caliskan Salihi E, Aydin E (2017). Adsorptive characteristics of isoniazid on powdered activated carbon: π–π dispersion interactions at the solid–solution interface. Journal of Dispersion Science and Technology, 38(4):457-462.
2. Caliskan Salihi E, Wang J, et al., (2016). Enhanced removal of nickel(II) ions from aqueous solutions by SDS functionalized graphene oxide. Separation Science and Technology, 51(8): 1317-1327.

P-516: INVESTIGATION OF THE ANTI-GENOTOXIC PROPERTIES OF METHİONİNE-SCHIFF BASE.

[1] Ozkan Hasanoglu, E., [2] Kizil, HE., [3] Yetim Kurnaz, N., [4] Sakiyan, I., [5] Agar, G., [1] Sari, N.

[1] Gazi University, Faculty of Science, Department of Chemistry, Teknikokullar, Ankara, Turkey

[2]Bayburt University, Central Research Laboratories Application and Research Center, Bayburt

[3]Kirklareli University, Faculty of Arts and Science, Department of Chemistry, Kirklareli, Turkey

[4]Ankara University, Department of Sciences, Ankara, Turkey

[5] Atatürk University, Faculty of Science, Department of Biology, Erzurum, Turkey

INTRODUCTION:

Mutagenic agents act through the production of free radicals and free radicals are damage to DNA. Antimutagens agents are capable to deactivate of radicals (1). So, new compounds demonstrating antimutagenic activities are of great practical importance, especially for cancer therapy. Numerous compounds are synthesized and investigated for their antimutagenic activities each year. The purpose of the research is to evaluate the genotoxic and anti-genotoxic properties of Methionine-Schiff base. The anti-genotoxic properties of this compound in human lymphocytes cells were investigated by sister chromatid exchanges (SCEs) test system against aflatoxin Bı (AFBı).

MATERIALS AND METHODS:

Cytogenetic Analysis; Peripheral blood lymphocytes were taken from four (two men and two women) non-smoking healthy individuals. Lymphocyte cultures were set up by adding 0.5 mL of heparinised whole blood to RPMI-1640 chromosome medium supplemented with 15% heat-inactivated fetal calf serum, 100 IU/Ml streptomycine, 100 IU/mL penicillin and 1% L-glutamine. Lymphocytes were stimulated to divide by 1% phytohaemaglutinin (2).

RESULTS:

SCE frequency significantly decreased after treatment with the different concentrations of (Met-Sch) in DMSO solution and AFBı. 5 µg/mL concentration of (Met-Sch) in DMSO solution was the most effective against AFBı.

CONCLUSIONS:

In the present study, it has been revealed that this compound is the active inhibitors of anti-genotoxic activity of AFBı. Antimutagenic effects of this compound is probably related to its action on the enzymatic activation system.

ACKNOWLEDGEMENTS:

This study was supported by G.U. Scientific Research Fund (Project number: 05/2010-03)

REFERENCES

1. Handique AK, Aprem H (1997). Curr Sci., 72: 578-580
2. Hasanoglu Ozkan E, Kizil HE, et al., (in press), G. U, Journal of Science.

P-517: MEH3 (TYR113HIS) POLYMORPHISM , RESPONSE TO CHEMOTHERAPY AND SURVIVAL IN NON-SMALL CELL LUNG CANCER PATIENTS

[1] Soydas, E., [1] Ada, AO., [2] Gulhan, M., [1] Iscan, M.

[1]Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Ankara, Turkey,

[2]Ataturk Pulmonary Diseases and Thoracic Surgery Training and Research Hospital, Ankara, Turkey

INTRODUCTION:

Microsomal epoxide hydrolase gene (EPHX1) contains polymorphisms which may be linked to several cancer types. (Tyr113His) polymorphism that located in exon-3 of human EPHX1 gene is associated with %50 decrease in enzyme activity. There are studies that investigate a relationship between mEH3 polymorphism and several cancers like breast, bladder, colon, esophageal, over and lung but they are limited and inconclusive. In addition, studies in regard to the association between mEH3 polymorphism and response to chemotherapy and survival in lung cancer patients are rather limited and inconclusive. In this study, we aimed to investigate the effects of mEH3 polymorphism on the response to platinum based chemotherapy and survival in advanced stage non-small cell lung cancer (NSCLC) patients.

MATERIALS AND METHODS:

The 136 patients with the mean age of 56 ± 9 (mean ± SD; range: 34-75) who had a histological diagnosis of primary NSCLC with stages III or IV, and who were treated with platinum based chemotherapy were enrolled in this study. The mEH3 Tyr113His (rs1051740) gene polymorphism was determined by Real-Time PCR method modified from Tranah et al., (2005). Chi-square analysis and Fisher exact tests were used to compare the distribution of genotypes between subgroups and response to chemotherapy. Hazard ratios (HRs) were estimated from a multivariate Cox proportional hazards model with adjustment for age, gender, smoking status, chemotherapy regimen, tumor stage and tumor histology.

RESULTS:

The mEH3 Tyr113His (rs1051740) polymorphism did not significantly influence the responses to platinum based chemotherapy. No significant associations were noted between the responses of genotypes to chemotherapy and age, sex, smoking status, chemotherapy regimen, tumor stage or histology. Mutant carriers of mEH gene did not significantly survive shorter or longer than the wild type carriers of the gene (mean survival of 17.4 months for wild type genotype and 21.6 months for heterozygous/ mutant genotype; p=0.906). Multivariate analysis also revealed no significant altered adjusted hazard ratio (HR) of death associated with mEH genotypes. (HR, 0.747; 95 % CI, 0.41-1.35, p=0.33).

CONCLUSIONS:

These results show that the mEH3 Tyr113His (rs1051740) gene polymorphism is not likely to be associated with response to platinum based chemotherapy and survival in the patients with advanced stage NSCLC.

REFERENCES

1. Tranah GJ, Chan AT, et al., (2005). Molecular Carcinogenesis, 44:21-30.

P-518: HISTOPATHOLOGICAL BRAIN TISSUE EVALUATIONS AFTER REPETITIVE LOW-DOSE KETAMINE ADMINISTRATIONS IN MICE

[1] Erdinc, M., [1] Kelle, I., [1] Akkoc, H., [1] Uyar, E., [2] Erdinc, L., [3] Nergiz, Y., [3] Seker, U.

[1]Dicle University Medical Faculty, Department of Medical Pharmacology, Diyarbakir, Turkey.

[2]Dicle University Medical Faculty, Department of Biochemistry, Diyarbakir, Turkey.

[3]Dicle University Medical Faculty, Department of Histology and Embryology, Diyarbakir, Turkey.

INTRODUCTION:

N-methyl-D-aspartate receptors (NMDAR) are known to have fundamental functions in the formation of long-term potentiation (LTP), long-term depression (LTD) and maintaining synaptic plasticity (1,2). An increase or decrease in the activity of glutamatergic receptors alters cognitive performance (3). Literature suggests that low-dose ketamine (an NMDA receptor antagonist) induces neuroprotection (4), while high doses and extended applications are related to neurodegenerative symptoms (5).

In this study, we aimed to perform histopathological evaluations of the mice brain tissue after repetitive low-dose ketamine administrations.

MATERIALS AND METHODS:

Male BALB/c mice weighted 30-40 gr were treated with S(+) ketamine (20 mg/kg) for a single time and six consecutive times. Drugs were freshly prepared, dissolved in %0.9 saline and given intraperitoneally (ip). After sacrification, mice brain were isolated and embedded in paraffin. The obtained coronal slices of a broad range brain areas were practiced to execute histopathological assessments.

RESULTS:

Histopathological assessments of ketamine administered group for six consecutive times has shown partial neurodegenerative symptoms including; loss of cerebellar Purkinje cells, perineural edema in pyramidal neurons, thrombosis in the

subpial vascular area and necrosis in hippocampal neurons. Furthermore, proliferation in oligodendria cells was observed in this group. A single application of ketamine did not alter the morphologic appearance of the brain tissue.

CONCLUSIONS:

Consecutive applications of low-dose ketamine did induce neurodegeneration while a single dose didn't alter the morphologic structure of the brain. Extensive research should be conducted with ketamine to reveal its effects on memory processes and to find therapeutic ways to minimize its side effects.

REFERENCES:

1. Lau C, et al., (2007). "NMDA receptor trafficking in synaptic plasticity and neuropsychiatric disorders." Nature Reviews Neuroscience 8.6 (2007): 413.
2. Liu L, et al., (2004). "Role of NMDA receptor subtypes in governing the direction of hippocampal synaptic plasticity." Science304.5673 (2004): 1021-1024.
3. Riedel G, et al., (2003). "Glutamate receptor function in learning and memory." Behavioural brain research 140.1-2 (2003): 1-47.
4. Bhutta AT, et al., (2012). "Ketamine as a neuroprotective and anti-inflammatory agent in children undergoing surgery on cardiopulmonary bypass: a pilot randomized, double-blind, placebo-controlled trial." Pediatric Critical Care Medicine 13.3 (2012): 328-337.
5. Huang L., et al., (2012). "Ketamine potentiates hippocampal neurodegeneration and persistent learning and memory impairment through the PKCγ–ERK signaling pathway in the developing brain." Brain research 1476 (2012): 164-171.

P-519: MONITORING OF ADVERSE EFFECTS OF PRESCRIBED DRUGS IN ERZINCAN PROVINCE

[1] Polat, EC., [2] Nemutlu, N., [3] Sarikaya, B., [4,5] Gumusel, B., [6,7] Kocer Gumusel, B.

[1]Erzincan University, Faculty of Pharmacy, Department of Clinical Pharmacy, Erzincan, Turkey;

[2]Turkish Medicines and Medical Devices Agency, Ankara, Turkey;

[3]Burak Pharmacy, Erzincan, Turkey;

[4]Erzincan University, Faculty of Pharmacy, Department of Pharmacology, Erzincan, Turkey;

5Lokman Hekim University, Faculty of Pharmacy, Department of Pharmacology, Ankara, Turkey;

6Erzincan University, Faculty of Pharmacy, Department of Toxicology, Erzincan, Turkey

7Lokman Hekim University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

INTRODUCTION:

Adverse drug reaction (ADR) reporting is an important component of the health system. ADRs are one of the major causes of morbidity and mortality during drug therapy and a major contributor to healthcare costs. Spontaneous reporting of ADRs by health-care professional is considered as one of the basic methods for the prevention and detection of new and serious adverse effects to drugs in market (1,2). In this study, it was aimed to determine the frequency of observed ADRs in Erzincan province; the pharmacotherapeutic drug groups causing the ADRs and the most frequently affected system-organ classes. Moreover, it was also planned to improve the awareness of patients about ADR reporting.

MATERIALS AND METHODS:

The research was carried out as a questionnaire survey conducted face to face with adult patients who applied to community pharmacies in Erzincan. A total of 252 survey were completed.

RESULTS:

6% (n=15) of the survey were found to include one or more ADRs. ADRs were evaluated according to the System Organ Classes and the most frequently affected system- organ classes by ADRs were determined to be gastrointestinal disorders (23,3%), followed by skin and subcutaneous tissue disorders (16,7%) and general disorders (10%). The drug groups most frequently caused the ADRs were "Respiratory system drugs" (20,5%), Alimentary tract and metabolism drugs (18%) and Anti-infective for systemic use (15,3%). 13.3 % (n=2) of ADR's determined were classified as serious. 26,7% of ADRs needed to be treated. The relationship of the ADRs with the suspected drugs were evaluated, and the relationship was determined as "probable" in 46,7% of the ADRs and "possible" in 53,3% of the ADRs. 43,3% of the detected ADRs were not found in the Summary of Product Characteristics (SmPC) of the drug and classified as "unexpected".

CONCLUSION:

This was the first study to determine the frequency of ADRs and the drugs more frequently associated with ADRs in Eastern Anatolia Region. The incidence of ADRs related to drugs in Erzincan was observed to be lower than the finding obtained from Ankara. The most common drug group causing ADRs and most frequently affected system-organ class were also different. Post-marketing surveillance is the most important tool for pharmacovigilance systems for early detection of unexpected and serious ADRs. Suspected adverse events can be minimized and prevented by monitoring and reporting ADRs.

REFERENCES:

1. Ozcan G, Aykac E, et al., (2016). Adverse Drug Reaction Reporting Pattern in Turkey: Analysis of the National Database in the Context of the First Pharmacovigilance Legislation. Drugs Real World Outcomes, 3(1): 33–43.
2. World Health Organization (2006). The Safety of Medicines in Public Health Programmes: Pharmacovigilance an essential tool. WHO Press, Switzerland

P-520: INVESTIGATION OF CYP1B1 (CYP1B1*2 M1AND M2) GENE POLYMORPHISMS IN A TURKISH POPULATION

Kargin Solmaz, FO., Ada, AO.

Ankara University, Faculty of Pharmacy, Department of Toxicology, Ankara ,Turkey

INTRODUCTION:

One of the most important groups of metabolic enzymes responsible for the elimination of toxic substances is the Cytochrome P450 (CYP). Changes in CYP expression are considered to be effective toxicological factors when many carcinogenic compounds are thought to be bioactivated by first-phase enzymes and this metabolic activation is carried out intensely by CYPs. CYP1B1, an important isozyme of this family, is involved in the formation of reactive estrogen metabolites and in the activation of environmental carcinogens such as polycyclic aromatic hydrocarbons (PAHs). There are 4 known alleles of the human CYP1B1 gene (namely CYP1B1*2, CYP1B1*3, CYP1B1*4 and CYP1B1*7) that cause changes in and enzyme activity. CYP1B1*2 has two linked polymorphism in exon 2, rs10012 and rs1056827, resulting in the Arg48Gly and Ala119Ser amino acid substitutions, respectively. Individuals with high CYP1B1 activity may be at high risk of certain cancers such as lung due to the excess bioactivation of carcinogens. It has been reported that the frequencies of polymorphic genes in different populations are different in various ethnic groups. There are a few studies on CYP1B1 polymorphism and there is no clear data about the frequency of this gene polymorphism in Turkish population. Therefore, in this study, we aimed to determine the CYP1B1*2 allele frequency in a Turkish population.

MATERIALS AND METHODS:

150 volunteer individuals who do not have a diagnosis of any cancer were included in our study. In order to evaluate the results in detail, all individuals filled their informed consent forms with a questionnaire containing age, gender, occupation, smoking, alcohol and coffee habits, nutritional patterns and other necessary information. CYP1B1 m1 and m2 mutations were determined by allele specific PCR method. The study was approved by the ethics committee of Ankara University.

RESULTS:

The frequency of Arg/Arg (wild type), Arg/Gly (heterozygous variant), Gly/Gly (homozygous variant) CYP1B1*2 m1 genotypes were 47.33%, 44.66% and 8%, respectively. The frequency of Ala /Ala (wild type), Ala/Ser (heterozygous variant), Ser/Ser (homozygous variant) CYP1B1*2 m2 genotypes were 42.85%, 42.85% and 14.28%, respectively.

CONCLUSIONS:

The results of this study will provide basic data in determining the extent of the effect of this polymorphic gene in cancer and various diseases in Turkish population prospectively by giving a comprasion with other populations.

ACKNOWLEDGEMENT

This study was supported by the Research Fund of Ankara University (Grant no: 10B3336003).

P-521: INVESTIGATION OF POLYMER COATED GOLD NANOPARTICLES INDUCED LIPID PEROXIDATION AND PROTEIN OXIDATION ON HEPG2 CELLS

[1,2] Sen, TG., [3,4] Ozkemahli, G., [2] Shahbazi, R., [3] Erkekoglu, P., [2,5] Ulubayram, K., [2,3,6] Kocer Gumusel, B.

[1]Baskent University, Biomedical Engineering Program, Ankara, Turkey

[2]Hacettepe University, Graduate Department of Nanotechnology and Nanomedicine, Ankara, Turkey

[3]Hacettepe University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

[4]Erzincan University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

5Hacettepe University, Faculty of Pharmacy, Department of Basic Pharmaceutical Sciences, Ankara, Turkey

6Lokman Hekim University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

INTRODUCTION:

With the rapid development of nanotechnology and the widespread use of nanoparticles in the biomedical area, the toxicity of nanomaterials has begun to attract attention.

Generally, toxicity originates from small size and high surface-to-volume ratio of nanomaterials. In comparison to similar ones with large structures, the nanoparticles can lead to higher intracellular reactive oxygen species (ROS) levels and cytotoxicity. Gold nanoparticles (AuNPs) are colloidal or clustered particles consisting of a gold core and a surface coating around the core. They are considered to be

outstanding delivery systems in medicine. In order to reduce their toxicity, it was suggested that their surface properties should be altered by various polymeric coatings. The aim of this study was to examine the effects of AuNPs induced cytotoxicity, lipid peroxidation and protein oxidation on HepG2 cells and investigate the toxicity modifying effects of “polyethylene glycol (PEG) and polyethylene imine (PEI) (molecular weights of 2000 (LMW) and 25000 (HMW)) coatings.

MATERIALS AND METHODS:

The study groups were determined as AuNPs, AuNPs/PEG, AuNPs/PEI LMW) and AuNPs/PEI HMW. Cytotoxicity was determined by MTT assay. Lipid peroxidation and protein oxidation were determined by using commercial spectrophotometric kits. Malondialdehyde (MDA) levels were measured as an indicator of lipid peroxidation and protein carbonyl levels were determined as an indicator of protein oxidation.

RESULTS:

After incubating HepG2 cells with different concentrations of nanoparticles for 24 h, half maximal inhibitory concentrations (IC50) were determined as 166.77, 257.73 and 198.44 µg/ml for AuNPs, AuNPs/PEG and AuNPs/PEI LMW groups, respectively. However, IC50 dose could not be determined in AuNPs/PEI HMW group due to high cytotoxic potential of PEI HMW. In AuNPs/PEI HMW group, MDA levels were 253.53% higher than control group and 311.17% higher than Au group ($p < 0.05$, both). The increases in carbonyl levels in AuNPs/PEG and AuNPs/PEI HMW groups were found be significantly higher than control (61.67% and 462.41%, respectively; $p<0.05$, both). The carbonyl levels measured in AuNPs/PEG, and AuNPs/PEI HMW groups were also higher than in the Au group (33.97% and 366.07%, respectively; $p<0.05$, both).

CONCLUSIONS:

These results suggest that PEG coating does not have an impact on cytotoxic and oxidative properties of AuNPs; however coating AuNPs with PEI (particularly by PEI HMW) can induce both cytotoxicity and oxidative stress. Therefore, coating materials of AuNPs should be chosen with caution in order not to increase the toxic effects of the nanoparticles.

P-522: A STUDY ABOUT ANTI-PROLIFERATIVE EFFECT OF A4B3 ON HUMAN LUNG CANCER CELLS (A549)

[1] Aydin, H., [2] Yumrutas, O., [3] Lolak, N., [3] Akocak, S.

[1]Adiyaman University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Adiyaman, Turkey

[2] Adiyaman University, Faculty of Medicine, Department of Medical Biology, Adiyaman, Turkey

[3]Adiyaman University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Adiyaman, Turkey

INTRODUCTION:

It is known that the death from cancer has been increasing day by day. According to a report published WHO (1), approximately nine million people died from cancer in 2015. Lung cancer is the first among the most common cancer types throughout the world. Current compounds for treatment of Lung cancer are yet too limited, and so new compounds should be developed. Previously, we have designed and synthesized a series of bis-sulfonamide Schiff bases as an efficient and potent carbonic anhydrase inhibitors, which are related to cancer detection and treatment. In the current work, the compound A4B3 was selected since it is one of the most efficient compounds from the series. Hence, the present study was designed to show the anti-proliferative effect of A4B3 on Human Lung Cancer Cells (A549).

MATERIALS AND METHODS:

In order to determine the anti-proliferative activity of the compound, MTT (3-[4,5- dimethylthiazol- 2-yl]- 2,5- diphenyl- tetrazolium bromide) method was used. A549 cells exposed to different doses of the compound (25, 50, 100 and 200 µl) at 37ºC with 5% CO2 for 24h.

RESULTS:

It was determined that anti-proliferative effect of the compounds was increased in a dose dependent manner.

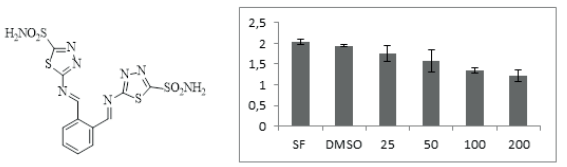


Figure 1. Chemical structure and anti-proliferative effect (µg/ml)

CONCLUSIONS:

Consequently, the compound has an anti-proliferative effect, but in order to make enough to explain about its anticancer activity, it should be examined by other test systems, including the methods such as apoptosis induction, cell cycle and so on.

REFERENCES:

1. http://www.who.int/mediacentre/factsheets/fs297/en/

P-523: ASSESMENT OF OXIDATIVE DNA DAMAGE IN CERAMIC WORKERS

[1] Anlar, HG., [2] Bacanli, M., [3] Iritas, S., [4] Tutkun, E., [5] Yilmaz, OH., [1] Basaran, N.

[1]Bulent Ecevit University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Zonguldak, Turkey

[2]Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Ankara, Turkey

[3]The Council of Forensic Medicine, Branch Office of Ankara, Ankara, Turkey

[4]Bozok Univesity, Faculty of Medicine, Department of Public Health, Yozgat, Turkey

5Yildirim Beyazit Univesity, Faculty of Medicine, Department of Public Health, Ankara, Turkey

INTRODUCTION:

Silica (SiO2) is an abundant mineral in rock, sand and soil (1). The International Agency for Research on Cancer (IARC) classified crystalline silica as a known human carcinogen (2). Occupational exposure to silica dust in workers is still considered to be an important health problem especially in developing countries. The present study aimed to investigate the plasma 8-hydroxy-2'-deoxyguanosine (8-oxodG) levels, a sensitive biomarker of oxidative DNA damage, in Turkish ceramic workers (3). The influence of confounding factors like age, smoking, alcohol drinking, duration of exposure on plasma 8-oxodG levels were also analyzed.

MATERIALS AND METHODS:

Blood samples were taken from the ceramic workers (n=99) and their controls (n=81). Each participant completed a detailed questionnaire. Plasma 8-oxodG levels (pg/ml) were determined by using kit at a wavelength between 405 and 420 nm.

RESULTS:

Plasma 8-oxodG levels of the workers were found to be significantly higher than the control group ($p<0.05$). Workers working in the ceramic plant more than 16 years and smokers had significantly higher plasma 8-oxodG levels when compared to the other workers ($p<0.05$). There were correlation between using alcohol, age and 8-oxodG levels, but it was not statistically significant. There was no correlation between using protective equipments and plasma 8-oxodG levels. Workers with silicosis have slightly higher 8-oxodG levels when compared to the other workers.

CONCLUSIONS:

These results showed that occupational silica exposure can cause oxidative DNA damage that may lead to important health problems in ceramic workers.

ACKNOWLEDGEMENTS:

This study was funded by The Scientific and Technological Research Council of Turkey (Project number: 115S079)

REFERENCES

1. Yassin A, Yebesi F, et al., (2005). Environ. Health Perspect, 113: 255-60.

2. International Agency for Research on Cancer (IARC). IARC monographs on the evaluation of carcinogenic risks to humans. Silica, some silicates, coal dust and para-aramid fibrils. Lyon: IARC; 1997.

3. Valavanidis A, Vlachogianni T, et al., (2009). J Environ Sci Health C Environ Carcinog Ecotoxicol Rev. 27(2):120-39.

P-524: THE RELATIONSHIP BETWEEN CYTOKINE GENE POLYMORPHISMS AND TYPE 2 DIABETES IN A GROUP OF TURKISH POPULATION.

[1] Ates, I, [2] Guvenc, A., [3] Altuner, D.,[1] Karakaya, A.

[1] Ankara University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

[2] Kırsehir City Hospital, Kırsehir, Turkey

[3] Erzincan University, Faculty of Medicine, Department of.Medicinal Pharmacology, Erzincan, Turkey

INTRODUCTION:

Type 2 diabetes is a hyperglycaemic metabolic disease related with the decrease of insulin secretion. Genetic and environmental factors are playing major role in the development of the disease. Relationship between the inflammation generation and diabetic complications has been showed in recent studies. Following the formation of the oxidative stress after the disorder of the lipid metabolism, the levels of the reactive oxygen species (ROS) increase and insulin resistance develops consequently. Cytokines are important in regulation of the homeostatic mechanisms such as inflammation and tissue repair. Thus, variations in their levels and structures can cause several diseases. The single nucleotide polymorphisms (SNP) forming on the cytokine genes increase the risk of disease development. Recent studies showed the relationship between some inflammatory cytokine gene polymorphisms and the development of complication in patients with diabetes. Based on this, our aim was searching and the evaluating the possible relations between the TNF-α (-308), IL-1β (+3953), IL-6 (-174) gene polymorphisms and the development of the complications in a Type 2 diabetic Turkish patient population by using PCR-

RFLP method.

MATERIALS AND METHODS:

A total of 150 Turkish individual participants were grouped in three groups as controls, patients with and withoutdiabetic complications consisting of 50 individuals in each. All the patients were selected from the the Diabetes Clinic at the Ankara Training and Research Hospital. 50 patients were free of complications, whereas the others suffered from complications including nephropathy, retinopathy, neuropathy and coronary heart disease. DNA samples of all the subjects were isolated from the blood samples and stored at -200C until the analysis. Genotyping was performed using a polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) technique.

RESULTS:

Due to our data, both TNF-α and IL-1β gene polymorphisms are significantly related with the development of both disease and complications.

CONCLUSIONS:

TNF-α and IL-1β gene variations enhance the risk of Type 2 diabetes and its complications development.

P-525: ASSESSMENT OF URINARY 8-HYDROXYL-2′-DEOXYGUANOSINE (8-OHDG) AND 1-HYDROXYPYRENE LEVELS AS BIOMARKERS OF EXPOSURE TO PAHS IN ELECTRONIC CIGARETTE (E-CIGARETTE) USERS

[1] Cok, I., [2] Koc Morgil, G., [1] Ali, AA.,[1] Ulutas, OK.,[3] Yilmaz, O., [1] Aysal, IA.

1Gazi University, Faculty of Pharmacy, Department of Toxicology, 06330, Hipodrom, Ankara, Turkey

[2] Minister of Health, General Directorate of Public Health, Department of Consumer Safety and Public Health Laboratories, Toxicology Laboratory, Sıhhıye, Ankara,Turkey

[3]Gazi University, Faculty of Pharmacy, 06330, Hipodrom, Ankara, Turkey;

INTRODUCTION:

Despite the recent popularity of e-cigarettes, to date only limited data is available on their safety and effectiveness for users. Recent chemical analysis of e-cigarettes has showed that variety toxicants and carcinogens were detected in the refill solutions and aerosols of e-cigarettes such as formaldehyde, metals, nitrosamines, acrolein, acetaldehyde and polycyclic aromatic hydrocarbons (PAHs). PAHs belong to a class of ubiquitous carcinogens and are possibly associated with adverse health effects. In this study, we aimed to assess PAH exposure by measuring the 1-hydroxypyrene (1-OHP) in urine samples of e-cigarette users and to explore the possible associations between PAH exposure and oxidative DNA damage indicated by urinary 8-hydroxy-2′-deoxyguanosine (8-OHdG). Urinary 8-OHdG and 1-OHP are biological markers of oxidative DNA damage and PAH metabolism, respectively. We investigated the relationship between urinary 8-OHdG and 1-OHP in e-cigarette users.

MATERIALS AND METHODS:

Between May 2016 and September 2017, spot urinary samples were collected from e-cigarette users (n:28), cigarette smokers (n:25), passive smokers (n:25) and healthy non smokers (n:25). Urinary 8-OHdG and 1-OHP levels were determined using Liquid chromatography tandem-mass spectrometry (LC-MS/MS) and expressed as ng/g creatinine.

RESULTS:

The urinary 1-OHP concentrations (mean± SD) has been found for cigarette smokers as 100.52±120.55, for e-cigarette users as 80.86±161.0, for passive smokers as 44.07±34.17 and for control group as 28.21±27.3 ng/g creatinine. Maximum value for 8-OHdG was recorded in cigarette smokers (22.97±10.34 ng/g creatinine) followed by e-cigarette smokers (16.59±12.56 ng/g creatinine) and passive smokers (15.62±10.83 ng/g creatinine) and controls (7.36±7.39 ng/g creatinine). 8-OHdG levels in e-cigarette users (16.59±12,56) were significantly higher (p>0,0023) than those of healthy controls group (7,36±7,39). Significantly higher level) of urinary 1-OHP(2.86-fold increase in mean 1-OHP values) and 8-OHdG (2.25-fold increase in mean 8-OHdG) was found among e-cigarette users compared to controls in this study. Individual urinary 8-OHdG concentrations were directly correlated with urinary 1-OHP concentrations for cigarette smokers (p=0.0461). For e-cigarette users this correlation was high but not statisticaly significant (p=0.1666).

CONCLUSIONS:

Our findings suggest that urinary 1-OHP and 8-OHdG reflect PAH exposure and oxidative DNA damage in cigarette smokers and e-cigarette users.

P-526: THE ANTIOXIDANT AND CYTOTOXIC ACTIVITIES OF TWO THYMUS SPECIES ESSENTIAL OIL

[1] Yaris, E., [2] Yigitkan, S., [3] Yener, I., [4] Alkan, H., [5] Firat, M., [3] Varhan Oral, E., [6] Yolcu, M., [6] Senturk, K., [7] Irtegun Kandemir, S., [1] Ertas, A.

[1]Dicle University, Faculty of Pharmacy, Department of Pharmacognosy, Diyarbakir, Turkey

[2]Dicle University, Faculty of Pharmacy Department of Pharmaceutical Botany, Diyarbakir, Turkey

[3]Dicle University, Faculty of Pharmacy, Department of Analytical Chemistry, Diyarbakir, Turkey

[4]Dicle University, Faculty of Pharmacy, Department of Biochemistry, Diyarbakir, Turkey

5Yuzuncu Yıl University, Faculty of Education, Department of Biology, Van, Turkey

6Dicle University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Diyarbakir, Turkey

7Dicle University, Faculty of Medicine, Department of Medical Biology, Diyarbakir, Turkey

INTRODUCTION:

The genus Thymus L. is a member of Lamiaceae family and represented by 318 species in the world, 40 species in Turkey and 18 of them are endemic for Turkey (45%) (1). In this study, it is aimed to determine the antioxidant activities and cytotoxic effects of essential oils obtained from T. brachychilus subsp. brachychilus and T. brachychilus subsp. bahcesarayensis.

MATERIALS AND METHODS:

In this study, the cytotoxic activity of essential oil of T. brachychilus subsp. brachychilus and T. brachychilus subsp. bahcesarayensis was determined by MTT method. Human-derived cancer cell series and the Primary Dermal Fibroblasts series were used in this study. For this purpose, the breast cancer cell line (MCF-7), the colon cancer series (HT-29) and the Primary Dermal Fibroblast Series (PDF) were provided (2). Aditionally, β-Carotene method, ABTS cation radical decolorisation method and DPPH free radical scavenging activity were carried out to indicate the antioxidant activity.

RESULTS:

In method β-Carotene, essential oil of T. brachychilus subsp. brachychilus was determinated more active. Also in ABTS cation radical decolorisation method and DPPH free radical scavenging activity methods, essential oil of T. brachychilus subsp. bahcesarayensis species was found more active. In the MCF-7 cell series, it was determinated that the eseential oil gained from T. brachychilus subsp. brachychilus species was highly active. In the MCF-7 cell series, it was determinated that the eseential oil gained from T. brachychilus subsp. brachychilus species was highly active. And in the HT-29 and PDF cell series it was determinated that the eseential oil gained from T. brachychilus subsp. bahcesarayensis species showed more cytotoxic activity.

CONCLUSIONS:

Generally it has been determined that obtained essential oils have high antioxidant and moderate cytotoxic potentials.

ACKNOWLEDGEMENTS:

The research was funded by grant: DUBAP ECZ.15.003

REFERENCES:

1. Baytop T (1994). Türkiye'de Tıbbi Bitkilerle Tedavi, Nobel Tıp Kitapevleri, Istanbul, Turkey
2. Ertas, et al., (2014). Pau. J. Agr. Food Chem. 62, 4601–4609.

P-527: THE CYTOTOXIC EFFECTS OF ESSENTIAL OILS OF FIVE SALVIA SPECIES ON THREE CELL LINES

[1] Yaris, E., [2] Yigitkan, S., [3] Firat, M., [4] Irtegun Kandemir, S., [5] Yener, I., [6] Alkan, H., [7] Senturk, K., [1] Ertas, A., [8] Kolak, U.

1Dicle University, Faculty of Pharmacy, Department of Pharmacognosy, Diyarbakir, Turkey

2Dicle University, Faculty of Pharmacy Department of Pharmaceutical Botany, Diyarbakir, Turkey

3Yuzuncu Yıl University, Faculty of Education, Department of Biology, Van, Turkey

4Dicle University, Faculty of Medicine, Department of Medical Biology, Diyarbakir, Turkey

5Dicle University, Faculty of Pharmacy, Department of Analytical Chemistry, Diyarbakir, Turkey

6Dicle University, Faculty of Pharmacy, Department of Biochemistry, Diyarbakir, Turkey

7Dicle University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Diyarbakir, Turkey

8Istanbul University, Faculty of Pharmacy, Department of General and Analytical Chemistry, Istanbul, Turkey

INTRODUCTION:

Since ancient times, plants belonging to the Labiatae family have been used for treating various diseases, including cancer, in many countries (1). In this study, it is aimed to determine the cytotoxic effects of essential oils obtained from Salvia multicaulis, S. spinosa, S. montbretii, S. suffruticosa and S. Xanthocheila in one healthy cell line (PDF) and two cancer cell line (MCF-7 and HT-29).

MATERIALS AND METHODS:

In this study, the cytotoxic activity of essential oils of S. multicaulis, S. spinosa, S. montbretii, S. suffruticosa ve S. xanthocheila were determined by MTT method. Human-derived cancer cell series and the Primary Dermal Fibroblasts series were used in this study. For this purpose, the breast cancer cell line (MCF-7), the colon cancer series (HT-29) and the Primary Dermal Fibroblast Series (PDF) were provided.

RESULTS:

While in the terms of the essential oils S. multicaulis showed a rather cytotoxic effect on MCF-7, S. spinosa showed cytotoxic effect on HT-29, S. suffruticosa showed highly cytotoxic effect both on HT-29 and MCF-7 and also S. xanthocheila showed cytotoxic effect on MCF-7 cell lines, also it has been determined that S. montbretii does not have cytotoxic effects on any cell line. In particular, it has been determined that the essential oil obtained from S. suffruticosa does not show toxicity on the healthy cell line but has a very high cytotoxic effect on MCF-7 and HT-29 (5% and 20% viability, respectively) cell lines at 200 µg / ml concentration.

CONCLUSIONS:

Generally it has been determinated that obtained essential oils have highly cytotoxic potentials. For this reason it can be said that the essential oil obtained from S. suffruticosa has especially more useful in the field of health.

REFERENCES:

1. Hartwell JL (1969). A survey. Loyldia 32: 247–296.

P-528: NOVEL LIGANDS FOR CANNABINOID RECEPTOR AND IN VITRO INVESTIGATION ON THEIR ANTIPROLIFERATIVE EFFECTS ON BRAIN TUMOR CELL LINE

[1] Kuzu, B.,[2] Taspinar, M., [1] Menges, N.

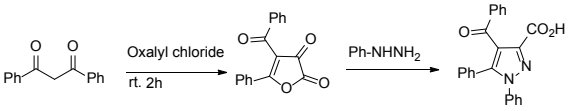
[1] Van Yuzuncu Yil University, Department of Pharmaceutical Chemistry, Van, Turkey

[2] Van Yuzuncu Yil University, Faculty of Medicine, Department of Medical Biology, Van, Turkey

INTRODUCTION:

Cannabinoid receptors found in two important systems of our body are involved in many vital and vital biological processes. These receptors are termed CB1 and CB2. CB1 is present in brain cells while CB2 is in the immune system (1). The rimonabant molecule used as a drug for this purpose and known to affect cannabinoid receptors is the tetrasubstitüed pyrazole derivative. Among the ligands used for cannabinoid receptors, the pyrazole ring plays an important role (2). In this work, four different poly-substituted pyrazole derivatives were synthesized using a suitable synthetic method.

MATERIALS AND METHODS:



The tetrasubstituted pyrazole molecules were synthesized according to the above synthesis steps and the in vitro effects were investigated by the MTT assay method.

RESULTS:

The effects of the synthesized compounds on the LN-405 cell line were examined. All compounds were found to have a similar biologic property and had a significant toxic effect on cell lines at concentrations of 0.01 µM.

CONCLUSIONS:

it was observed that cell proliferation was triggered and cells were excessively increased when concentrations exceeded 0.01 µM in all the molecules. At concentrations of 0.01 µM antiproliferation was observed in the compounds at approximately 20-30%. Further experiments are needed to determine which mechanism of antiproliferation and / or proliferation is working.

ACKNOWLEDGEMENTS:

This work was supported by Yüzüncü Yıl University Scientific Research Projects Coordinator (2015-SBE-YL236).

REFERENCES:

1. Marsicano G (2008). Köfalvi A (ed). Cannabinoids and The Brain, Boston, MA: Springer US, pp 161–201.
2. Mackie K (2008). J. Neuroendocrinol. 20: 10-14.

P-529: CYTOTOXIC EFFECTS OF BARIUM SULFATE (BASO4) NANOPARTICLES IN A549 CELLS

[1] Bacanli, M., [2] Schumann, B., [2] Glahn, F.,[2] Thomas, S., [2] Foth, H., [1] Basaran, N.

[1] Hacettepe University, Department of Pharmaceutical Toxicology, Ankara, Turkey

[2] Martin Luther University, Istitute of Environmental Toxicology, Halle (Saale), Germany

INTRODUCTION:

Nano sized materials are increasingly used in the fields of industry, science, pharmacy, medicine, electronics, communication and consumer products (1). However, there is still considerable lack of information about the toxicity of some NPs. Barium sulfate nanoparticles (BaSO4 NP) are widely used in as fillers in coatings, orthopedic medicine, diagnostic medicine and other applications (2). This presentation aims to investigate

the possible cytotoxic effects of BaSO4 NP in human lung adeocarcinoma cell line (A549).

MATERIALS AND METHODS:

the reaction of lung cells to particle exposure (24 h and 72 h) was measured as cytotoxicity by resazurin assay.

RESULTS:

A concentration dependent decline was seen in the viability of cells exposed to BaSO4 NP in both exposure times. After 24 h incubation, cell viability was further reduced when compared to 72 h incubation. The concentrations of BaSO4 NP up to 0,005 mg/ml did not affect the viability of A549 cells in both incubation periods. However, at the concentration of 0,25 mg/ml, the cell viability decreased significantly.

CONCLUSIONS:

According to our results, it seems that BaSO4 NP are cytotoxic against human lung cancer cells. Nevertheless, he mechanism behind these effects deserves further clarification.

ACKNOWLEDGEMENTS:

This study was funded by a grant from The Scientific and Technological Research Council of Turkey (Project number: 2219 International Post Doctoral Research Fellowship Programme).

REFERENCES:

1. Arora S, Rajwade JM, et al., (2012). Toxicology and Applied Pharmacology, 258(2):151-165.
2. Noreen R, Pineau R, et al., (2011). Analytical and Bioanalytical Chemistry, 401(3):795-801.

P-530: INTERACTIONS OF CURCUMIN WITH CISPLATIN ON V79 CELL VIABILITY

[1] Becit, M., [1] Aydin, S., [2] Basaran, AA., [1] Basaran, N.

[1] University of Hacettepe, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Ankara, Turkey

[2] University of Hacettepe, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Turkey

INTRODUCTION:

It is believed that some natural compounds might reduce the development of cancer through the antioxidant activity. Curcumin (CUR) obtained from Curcuma longa is commonly administered as a dietary antioxidant food supplement. The anticancer effect of CUR has been great concern in many researches. Cisplatin is known to be one of the chemotherapeutic drugs used in the therapy of many solid tumors. In the treatment of cancer, plant-derived phenolic compounds are suggested to be used with various chemotherapeutic drugs to increase anticancer effect and decrease cytotoxicity. Since the mechanisms of the interactions of CUR with cisplatin are not well clarified, we aimed to determine the effects of CUR on cisplatin cytotoxicity in Chinese lung fibroblast cell lines (V79) (1,2).

MATERIALS AND METHODS:

MTT assay was used to determine the cell viability for 24 h and 48 h.

RESULTS:

The IC50 values of CUR were found to be 877 μM and 119 μM for 24h and 48h, respectively. CUR (1.71 fold at 1000 μM, for 24 h; 2.08 fold, 3.07 fold, 7.77 fold, and 14.76 fold at 125 μM, 250 μM, 500 μM and 1000 μM, respectively, for 48 h vs. IC50 doses of cisplatin) significantly increased the cytotoxicity of cisplatin in a dose dependent manner.

CONCLUSIONS:

It seems that curcumin may affect the cytotoxicity of cisplatin and have an important interaction with cisplatin in the chemotherapy; however, further in vitro and in vivo studies are required to confirm their interactions with cisplatin.

ACKNOWLEDGEMENTS:

The authors declare that there are no conflicts of interest.

REFERENCES

1. Bansal SS, et al., (2011). Advanced drug- delivery systems of curcumin for cancer chemoprevention. Cancer Prev Res, 4(8):1158-71.
2. Perrone D, et al., (2015). Biological and therapeutic activities and anticancer properties of curcumin. Exp Ther Med, 10(5):1615-23.

P-531: THE POSSSIBLE ASSOCIATION BETWEEN BRAIN-DERIVED NEUROTROPHIC FACTOR GENETIC POLYMORPHISM VAL66MET AND SUSCEPTIBILITY TO BIPOLAR DISORDERS

[1] Demirbugen, M., [2] Hosgoren, Y., [3] Duman, B., [3] Baskak, B., [3] Devrimci Ozguven, H., [1] Suzen, HS.

[1] Ankara University, Department of Pharmaceutical Toxicology, Ankara, Turkey

[2] Golbası Sehit Ahmet Ozsoy Public Hospital, Ankara, Turkey

[3] Ankara University, Department of Psychiatry, Ankara, Turkey

INTRODUCTION:

Bipolar disorder (BPD) is a chronic severe neuropsychiatric disorder, with high lifetime prevalence [1]. Despite recent investigations and new researches, the exact mechanism of BPD is still unknown. Besides physiological and environmental factors, genetic factors play important role in the development of BPD. The brain-derived neurotrophic factor (BDNF), might be an interesting candidate

gene for bipolar disorder because of its important role in the neurodevelopment of the central nervous system[2]. The G to A transition in exon 5 of the BDNF gene, results valine substitution to methionine amino acid. This change results in BDNF functional polymorphisms in this region as Val66Val, Val66Met, and Met66Met genotypes and might be associated with the susceptibility to the BPD. On this basis, our aim was to evaluate the association between Val66Met polymorphism in BDNF gene and susceptibility to the BPD.

MATERIALS AND METHODS:

Genomic DNA was isolated from 28 control subjects and 30 BPD patients. The BDNF gene Val66Met polymorphism analyzed by using PCR-RFLP technique. Genotypes and allele frequencies were compared between groups using Chi-square test.

RESULTS:

We have found that, the frequency of the Val allele was lower in BPD patients when compared to the healthy control subjects. (X2=1.16, p=0.28, OR=1.97 95%CI=0.49-8.19).

CONCLUSIONS:

The present study demonstrated that the BDNF gene Val66Met polymorphism might be associated with susceptibility to the BPD. However, there is no compelling evidence of BDNF gene playing an important role in susceptibility to BPD as sex, onset age, comorbidity, impairment in brain morphology and function have also role in the occurrence.

REFERENCES:

1. Phillips MR, et al., (2009). Prevalence, treatment, and associated disability of mental disorders in four provinces in China during 2001-05: an epidemiological survey. Lancet, 2009. **373**(9680): p. 2041-53.
2. Fan J, Sklar P (2008). Genetics of bipolar disorder: focus on BDNF Val66Met polymorphism. Novartis Found Symp, 2008. **289**: p. 60-72; discussion 72-3, 87-93.

P-532: DETERMINATION OF REGIONAL DIFFERENCES IN THE ADVERSE DRUG REACTIONS OBSERVED IN ANKARA PROVINCE

[1,2] Nemutlu, N., [2,3] Kocer Gumusel, B.

[1]Turkish Medicines and Medical Devices Agency, Ankara, Turkey;

[2]Hacettepe University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

[3]Lokman Hekim University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

INTRODUCTION:

Pharmacovigilance is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem. The main aim of pharmacovigilance is to enhance patient care and patient safety in relation to the use of medicines. When the both negative effects of adverse drug reactions (ADR) on the human health and magnitude of the resources spent for treatment of the noxious effects of drugs were considered, importance of the prediction and prevention of the potential unintended effects of drugs are understood. Drug-related problems, including ADR, can vary between countries and even regions. In this study, it was aimed to collect data for the frequency of observed ADR in Ankara province and to identify possible regional differences for the drug groups causing the ADRs and the most frequently affected system-organ classes (1-3).

MATERIALS AND METHODS:

The research was carried out as a questionnaire survey conducted face to face with patients who applied to pharmacies determined by random sampling method in Cankaya, Yenimahalle and Elmadag.

RESULTS:

A total of 428 questionnaires [170 questionnaires (39,7%) in Cankaya, 127 questionnaires (29,7%) in Yenimahalle and 131 questionnaires (30,6%) in Elmadag region] were completed. 21.8% of the questionnaires in Cankaya, 18.9% of the questionnaires in Yenimahalle and 17.6% of the questionnaires in Elmadag region included one or more ADRs. When the ADR's were evaluated according to the System Organ Classes, it was determined that the most frequently affected system-organ class were "Gastrointestinal Disorders" in Yenimahalle and Elmadag (7.9%-5.3%), "Skin and Subcutaneous Tissue Diseases" (8,2%) in Cankaya. The drug groups most frequently caused the ADRs were also classified according to ATC groups. Musculoskeletal System Drugs (4.1%) in Cankaya, Anti-infectives for systemic use in Yenimahalle and Elmadag (5,5%, 5,3%) were in the first place.

CONCLUSION:

The frequency of ADRs and the drugs more frequently associated with ADRs were identified for the first time in the different regions of Ankara and some differences were detected between the regions. The causes of these differences may be related to the average age of the inhabitants of the region, disease distributions observed, drug use practices / habits, and dietary habits that differ by region and consumption of plant products (3).

REFERENCES:

1. Van Grootheest K (2003). The dawn of pharmacovigilance. Int J Psychiatry Med Int J Pharm Med., 17(5-6):195-200.
2. Marques J, Ribeiro Vaz I, et al., (2014). A survey of spontaneous reporting of adverse drug reactions in 10 years of activity in a pharmacovigilance centre in Portugal. Int J Pharm Pract Res., 22(4):275-82.
3. Alomar MJ (2014). Factors affecting the development of adverse drug reactions (Review article). Saudi Pharm J., 22(2):83-94.

P-533: EVALUATION OF OXYDATIVE LIPID AND CHOLESTEROL DAMAGES IN SILICOSIS

[1] Aksu, N., [2] Samadi, A., [2] Lay, I., [1] Nadir Ozis, T., [1] Sabuncuoglu, S.

1. Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Ankara, Turkey
2. Hacettepe University, Faculty of Medicine, Department of Medical Biochemistry, Ankara, Turkey

INTRODUCTION:

Silicosis is one of the prolonged and irreversible occupational diseases. Oxidative stress plays a role in many lung diseases including silicosis. Oxysterols are molecules that result in the oxidation of cholesterol. Oxysterols are formed by enzymatic and non-enzymatic reactions. Enzymatic derivatives act in the regulation of biological activities. Non-enzymatic derivatives are related to different pathologies. For this reason, these molecules can be used as biomarkers in the diagnosis and monitoring of diseases. The aim of the study is to evaluate possible cholesterol oxidation in silicosis by measuring 7-KC and triol levels and investigation of lipid peroxidation.

MATERIALS AND METHODS:

In this study, blood and urine samples were collected from 47 silicosis patients and 30 controls. 7-ketocholesterol (7-KC) and cholestane-3β, 5α, 6β-triol (Triol) levels were measured using HPLC-MS/MS. In order to evaluate lipid peroxidation, 8-isoprostane, human-4-hydroxynonenal (4-HNE) and human malondialdehyde (MDA) levels were determined by commercial ELISA kits.

RESULTS:

The measured levels of 7-KC were 40,61 ± 2,07 ng/ml and 20,26 ± 1,38 ng/ml. in silicosis patients and control group respectively. Triols were measured as 16,15 ± 2,22 ng/ml in the patients and 13,83 ± 1,75 ng/ml in the control group ($p<0,001$; $r=0,494$). The measured levels of plasma and urine human-8-isoprostane, 4-HNE and MDA levels were significantly higher in silicosis patients compare to control group. ($p<0.01$)

CONCLUSIONS:

Increased plasma 7-KC and Triol levels in silicosis may presumably be a result of increased LDL oxidation in these patients. 7-KC and Triol levels were moderately correlated in all groups. In addition lipid peroxidation significantly increased depending on oxidative stress in silicosis patients. The results confirm that cholesterol auto-oxidation can occur in silicosis as a result of oxidative stress induced inflammation. Any possible metabolic role of cholesterol oxidation products in silicosis warrants further research considering the tremendous nuclear effects of these oxysterols.

P-534: BENEFICIAL EFFECTS OF B-GLUCAN AGAINST CISPLATIN SIDE EFFECTS ON THE KIDNEY TISSUE.

[1] Taslidere, A., [2] Ciftci,O., [3] Turkmen, NB., [4] Kaya,K., [1] Gul, CC.

[1] Inonu University, Department of Histology and Embryology, Malatya, Turkey

[2] Pamukkale University, Department of.Pharmacology,Denizli, Turkey

[3]Inonu University, Department of Pharmaceutical Toxicology, Malatya,Turkey

[4] Adıyaman University, Department of Biıochemistry, Adıyaman,Turkey

INTRODUCTION:

To investigate the protective effect of Beta glucan (βg) on cisplatin (CP)-induced nephrotoxicity in rats.

MATERIALS AND METHODS:

Twenty eight rats were randomly distributed into four groups. The first group was kept as a control. In the second group, CP was given at the single dose of 7 mg/kg intraperitoneally. In the third group, βg was orally administered at the dose of 50 mg/kg/day for 14 days. In the fourth group, CP and βg were given together at the same doses.

RESULTS:

CP treatment caused significant oxidative damage via induction of lipid peroxidation and reductions antioxidant defense system potency in the kidney tissue. In addition, histopathological damage increased with CP treatment. On the other hand, βg treatment largely prevented oxidative and histopathological negative effects of CP.

CONCLUSIONS:

Cisplatin has severe nephrotoxic effects in rats and βg supplementation has significant beneficial effects against CP toxicity depending on its antioxidant properties. Thus, it appears that βg might be useful against CP toxicity in patients with cancer in terms of nephrotoxic system.

REFERENCES:

1. Kamisli S, Ciftci O, et al., (2014). Fish oil protects the peripheral and central nervous systems against cisplatin-induced neurotoxicity. Nutr Neurosci. 17(3):116-26.

P-535: BENEFICIAL EFFECTS OF DIOSPHORUS LOTUS AGAINST CISPLATIN SIDE EFFECTS ON THE HEARTH TISSUE

[1] Ciftci, O., [2] Turkmen, NB., [3] Taslidere, A., [3] Gul, CC.

[1]Pamukkale University, Department of.Pharmacology, Denizli, Turkey

[2]Inonu University, Department of Pharmaceutical Toxicology, Malatya,Turkey

[3]Inonu University, Department of Histology and Embryology, Malatya, Turkey

4Adıyaman University, Department of Biıochemistry, Adıyaman,Turkey

INTRODUCTION:

Hearth toxicity induced by anticancer chemotherapy is not uncommon, but underestimated and under-reported.Cisplatin (CP), a heavy metal compound, is used in the treatment of many types of tumours. The aim of this study was to investigate the possible beneficial effects of Diosphorus Lotus (DL) on hearth tissue oxidative status and histological alterations against CP-induced in the rats.

MATERIALS AND METHODS:

Twenty-eight male rats were randomly divided into four groups: group 1 - control, given isotonic saline solution; group 2 - CP 7 mg kg(-1) given intraperitoneally as single dose; group 3 - DL 1000 mg kg(-1) per day given orally for 10 days; group 4 - CP and DL given together at the same doses

RESULTS:

CP caused a significant increase in thiobarbituric acid-reactive substances (TBARS) level and a significant decrease in superoxide dismutase (SOD), glutathione peroxidase (GPx), catalase (CAT) and glutathione (GSH) levels in rats hearth tissues compared to the control group. CP caused a significant increase in lipid peroxidation in hearth tissues compared to the control group, whereas DL led to a significant increase in SOD and GSH levels. In addition histological changes were increased with CP. However, these effects of CP were eliminated by DL treatment.

CONCLUSIONS:

In conclusion, our study demonstrated that the hearth toxicity caused by CP may be prevented by DL treatment.

REFERENCES:

1. Kamisli S, Ciftci O, et al., (2014). Fish oil protects the peripheral and central nervous systems against cisplatin-induced neurotoxicity. Nutr Neurosci. 17(3):116-26.

P-536: EVALUATION OF GENOTOXIC EFFECTS IN ORAL MUCOSAL CELLS UNDERGOING NICKEL-TITANIUM ORTHODONTIC ARCHWIRES THERAPY

[1] Cetinkaya, S., [1] Erdem, O., [2] Kaplan, M., [3] Cirak, E., [4] Gokce, S., [3] Akay, C.

[1]Universities of Health Sciences, Department of Pharmaceutical Toxicology, Ankara, TURKEY

[2]Universities of Health Sciences, Department of Orthodontics, Ankara, TURKEY

[3]Retired

4Medipol University, Department of Orthodontics, Mega Hospitals Complex, Istanbul, TURKEY

INTRODUCTION:

Nickel-Titanium Archwires (Ni-Ti) materials which are metal alloy products are frequently used for the treatment of the dental structural defects (1). However, little is known about the possible genotoxic effects of using these devices in children who consider them as sensitive. Therefore, the aim of the study is to investigate the genotoxic effects of fixed orthodontic devices by micronucleus (MN) test in children using orthodontic devices.

MATERIALS AND METHODS:

This study was conducted in the Department of Orthodontics and Toxicology in Gulhane Military Medical Academy. 32 volunteer subjects of both sexes (16 women, 16 men), aged 12-17, provided informed consent and agreed to participate. Right and left buccal epithelial cells were collected from 32 patients at 0th as control and 7th, 15th, 30th, 45th, 60th and 90th days after placement of fixed appliances. The samples were stained with feuellgen reaction and fast-green techniques. Micronuclei frequency was scored for each slide sample in total 1000 cells. The

frequency result was determined per thousand (‰). The criteria by Tolbert et al. (2) and Thomas et al. (3) were adopted in the evaluation.

RESULTS:

The mean MN frequencies were significantly increased in day 7, 15, 30, 45 and 90 experimental groups when we consider compared to day 0 ($p<0.05$). MN frequencies in day 60 were determined as nearly same levels in day 0 and there is no statistically significant difference between in day 0 and 60. On the other hand, MN frequencies in day 90 were significantly lower than day 0 ($p<0.05$).

CONCLUSIONS:

Using of fixed orthodontic appliances induce increased MN frequency especially in the first weeks of treatment period due to the corrosion of the materials. However, these genotoxic effects tends to approach baseline levels in later period.

REFERENCES:

1. Wataha JC (2000). The Journal of prosthetic dentistry, 83(2): 223-234.
2. Tolbert PE, Shy CM, et al., (1992). Mutation Research, 271(1): 69-77.
3. Thomas P, Holland N, et al. Nature protocols, 4(6): 825-837.

P-537: INVESTIGATION OF TRACE ELEMENT LEVELS IN PATIENTS WITH FANCONI APLASTIC ANEMIA

[1] Erdem, O., [1] Cetinkaya, S., [2] Cirak, E., [3] Bayhan, T., [3] Unal, S., [3] Gumruk, F., [4] Eker, I.

[1]Universities of Health Sciences, Department of Pharmaceutical Toxicology, Ankara, TURKEY

[2]Retired

[3]Hacettepe University, Faculty of Medicine, department of Pediatric Hematology, Ankara, TURKEY

4Afyon Kocatepe University, Medicine Faculty, Department of Pediatric Hematology, Afyon, TURKEY

INTRODUCTION:

Fanconi aplastic anemia (FAA) is a rare bone marrow failure that is inherited autosomal recessive. Many congenital anomalies may accompany and various complications such as cancer and endocrinopathies may develop with FAA. Although trace element levels were investigated for different chronic diseases, there are no detailed studies and data for FAA patients. In this respect, the aim of this study was to investigate some trace element levels in FAA patients.

MATERIALS AND METHODS:

The study was carried out between June 2015 and April 2016 in patients with a confirmed FAA diagnosis. 17 patients selected as FAA group and 16 subjects were selected as control group in this study. The levels of copper (Cu), zinc (Zn), iron (Fe) cobalt (Co), chromium (Cr), selenium (Se) was measured using the method of graphite furnace atomic absorption spectroscopy (GFAAS). The results of experimental group were compared with the control groups.

RESULTS:

Median age of the patients was nine years (1-30), male to female ratio was 9/8. One of the patient underwent stem cell transplantation and four patients were transfusion dependent. When we analyze our results for control and FAA groups, we found that Cr and Cu levels in FA group were significantly higher than control group ($p<0.05$). In contrast to this Se levels of FAA group were significantly lower than those of control group ($p<0.001$). The levels of Cr and Se were found in the normal range for both of the groups. However, Cu levels were found outside of normal range in two samples from FAA patients and control subjects.

CONCLUSIONS:

In our study, we found a higher Cr and Cu levels in FAA patients compared to control group. We believe that the changes in trace element and toxic metal levels should be taken into consideration as regards the FAA patients when we consider our results. But, it is obvious that further studies are necessary to clarify this aspects and to explore the possible causes of the changes of homeostasis of bioelement levels.

P-538: PRELIMINARY SCREENING OF METHANOL EXTRACTS OF VIOLA SP. FOR ANTI-TYROSINASE ACTIVITY

[2] Ozbay, O., [1] Yilmaz Sarialtin, S., [2] Koroglu, A., [1] Coban, T.

[1] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Ankara, Turkey

[2] Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

INTRODUCTION:

Melanogenesis is a physiological process resulting in the biosynthesis of melanin pigments which are responsible for hyperpigmentation. The control of melanogenesis is an important strategy in the treatment of abnormal skin pigmentation for cosmetic purposes. Tyrosinase is one of the key enzymes in melanin biosynthesis and its inhibitors have become increasingly popular owing to their potential use as hypopigmenting agents especially in cosmetic

industry (1). However, most of them are unsatisfactory due to the weak clinical effects and/or to the various safety concerns (2,3). Therefore, it seems important to find out new tyrosinase inhibitory molecules. The aim of the present study was to investigate the anti-melanogenic effect of 9 different Viola sp methanol extracts by using mushroom tyrosinase assay.

MATERIALS AND METHODS:

Mushroom tyrosinase inhibitory activity of the extracts was carried out according to the standard method with minor modifications (4). The results were expressed as IC50±SD and s*tatistical analysis was performed using SPSS*v.25.0.

RESULTS:

All the tested extracts showed inhibitory effects against tyrosinase. Viola sieheana demonstrated the highest anti-tyrosinase activity among the other extracts (IC50:0,10 mg/ml) followed by Viola occulta with IC50 values of 0,21 mg/ml.

CONCLUSIONS:

Most of the tyrosinase inhibitors derived from higher plants such as polyphenols, flavonoids, aldehydes and their derivatives (3). *Further experiments* are *necessary* in order to evaluate and fractionate the active components responsible for the inhibition activity. These molecules might be useful in the food industry as antibrowning agents or in the medical field to treat hyperpigmentation disorders.

REFERENCES:

1. Pillaiyar T, et al., (2017). J Enzyme Inhib Med Chem. 32(1):403-425.
2. Dooley TP (1997). J Dermatol Treat. 8:275–279.
3. Curto EV, et al., (1999). Biochem Pharmacol. 57(6):663-72.
4. Souza PM, et al., (2012). PLoS One. 7(11):e48589.

P-539: SYNTHESIS AND ANTIOXIDANT ACTIVITY OF SOME PYRAZOLINE DERIVATIVES

[1] Evranos Aksoz, B., [2] Yilmaz Sarialtin, S., [2] Coban, T.

[1]Medicines and Medical Devices Agency, Analyses and Control Laboratories, Ankara, Turkey

[2] Ankara University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

INTRODUCTION:

Overproduction of free radicals can cause damage to biomolecules such as lipids, proteins, enzymes and DNA in cells and tissues. This may result in many diseases such as: cancer, diabetes, aging, cardiovascular, autoimmune, neurodegenerative disorders. Antioxidants are important compounds that reduce or neutralize the free radicals, thus protecting the cells from oxidative injury (1). Therefore, considerable research has been directed towards the identification of new antioxidants to prevent radical-induced damage. Pyrazoline derivatives are acknowledged to possess a wide range of bioactivities such as anti-inflammatory (2), anticancer and antioxidant (3). In pursuing the antioxidant potential of pyrazolines, we synthesized some pyrazoline derivatives and screened them for their antioxidant activity.

MATERIALS AND METHODS:

The in vitro antioxidant effect of some pyrazoline derivatives was determined by 2, 2'-azino-bis(3-ethylbenzthiazoline-6-sulphonic acid (ABTS•+) (4) and 2,2, diphenyl-1-picrylhydrazyl (DPPH•) (5) radical scavenging capacity assays.

RESULTS:

Previously reported eight 2-pyrazoline derivatives have been screened for their antioxidant activity. All tested compounds except (3-(3,5-dichloro-2-hydroxyphenyl)-5-p-tolyl-4,5-dihydropyrazol-1-yl) (phenyl)methanone (BEA 23) and (3-(3,5-dichloro-2-hydroxyphenyl)-5-p-tolyl-4,5-dihydropyrazol-1-yl) (furan-2-yl)methanone (BEA 24) showed ability to capture ABTS.+ free radical. Only compounds (3-(5-bromo-2-hydroxyphenyl)-5-(2-methoxyphenyl)-4,5-dihydropyrazol-1-yl)(pyridin-4-yl)methanone (BEA 1) and (3-(5-chloro-2-hydroxyphenyl)-5-(2-methoxyphenyl)-4,5-dihydropyrazol-1-yl)(pyridin-4-yl) methanone (BEA 2) showed ability to capture DPPH. free radical.

CONCLUSIONS:

(3-(3,5-dichloro-2-hydroxyphenyl)-5-(2-methoxyphenyl)-4,5-dihydropyrazol-1-yl)(pyridin-4-yl) methanone (BEA12) (IC50 = 0.09 mM) revealed the highest antioxidant potential for ABTS.+. The value is comparable with that of standard trolox (IC50 = 0.05 mM).

REFERENCES:

1. Uttara B et al (2009). Current Neuropharmacology, 7: 65-74.
2. Aggarwal R et al (2013). European Journal of Medicinal Chemistry, 70: 350-357.
3. Dinesha et al (2015). European Journal of Medicinal Chemistry, 104: 25-32.
4. Re R et al (1999). Free Radical Biology Medicine, 26(9-10):1231-1237.
5. Blois MS (1958). Nature, 29:1199-1200.

P-540: INVESTIGATION OF DNA-DAMAGING EFFECT OF C. CASSIA CHLOROFORM EXTRACT IN HL-60 CELLS

Sozer Karadagli, S., Agrap, B., Lermioglu Erciyas, F.

Ege University, Department of Toxicology, İzmir, Turkey

INTRODUCTION:

Cinnamomum cassia (C. cassia) leaves and bark extracts have several biological activities including antioxidant, antidiabetic, antimicrobial, and, antitumor effects(1). In our previous studies, we showed that C. cassia chloroform extract (CcCE) was effective against H2O2-induced increase of ROS levels in V79 cells, while it increased H2O2-induced oxidative DNA damage in these cells. However, we also showed the protective effect of CcCE in human lymphocytes using Comet assay (2). In the present study, we aimed to investigate the effect of CcCE in human promyelocytic leukemia (HL-60) cells.

MATERIALS AND METHODS:

HL-60 cells were treated with different concentrations of chloroform extract (0,78-100 µg/mL). Cytotoxic effect was determined by WST-1 test, at 24 hours intervals for three days. The extent of DNA damage was evaluated by alkaline comet assay (3) in HL-60 cells. For each concentration, 100 randomly selected cells (50 cells from each of the two replicate slides) were analyzed using comet analysis software (Comet Score 15, Tritek Corp.). The DNA damage was represented by percentage of DNA in the tail (tail DNA %).

RESULTS:

IC50 values of the extract were 6.27, 5.97 and 6,24 µg/mL for 24, 48 and 72 h incubation periods, respectively. Comet assay results indicated significant ($p<0,05$) and concentration-dependent increase of DNA damage in CcCE-treated HL-60 cells compared to controls.

CONCLUSIONS:

Our results display anti-cancer function of CcCE due to its cytotoxic and DNA damaging effects in HL-60 cells. Further in vitro and in vivo studies are necessary to confirm the chemopreventive potential of CcCE, at least in leukemia.

ACKNOWLEDGMENTS

This study was supported by Ege University Coordinatorship of Scientific Research Projects (11-ECZ 002 and 13-ECZ 014).

REFERENCES:

1. Rao PV, Gan SH (2014). Evidence-Based Complementary and Alternative Medicine, 2014: **642942, 12 pages**.
2. Agrap B (2013).Master Thesis. Investigation of the effects of *C. Cassia* bark extracts on oxidative stress, cytotoxicity, and DNA damage by Flow Cytometry and Comet Assay.
3. Collins AR (2004). Molecular Biotechnology. 26(3):249–261.

P-541: EFFECT OF METFORMIN ON THE OXIDATIVE DNA DAMAGE IN HUMAN LIVER CANCER CELLS

Cal, T., Sariaydin, T., Aydin, S., Undeger Bucurgat, U.

University of Hacettepe, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Ankara, Turkey

INTRODUCTION:

Type 2 diabetes is the most common form of diabetes. Metformin is a prescription drug commonly used for treating type 2 diabetes in adults and children (1). Metformin has been suggested to be responsible for anti-cancer activity via enhancing oxidative DNA damage under oxidative condition (2). However there are contradictory results in the literature. This study was aimed to evaluate the cytotoxic and genotoxic effects of metformin in human liver cancer (HepG2) cells.

MATERIALS AND METHODS:

The cytotoxicity of metformin (0.5-64 µM) was determined by Thiazolyl Blue Tetrazolium Blue (MTT) assay and its genotoxicity (5-1000 µM) was evaluated by alkaline comet assay in HepG2 cells treated with/without H2O2. DNA damage was expressed as DNA tail intensity.

RESULTS:

The cell viability significantly decreased at the doses above 4 µM. The IC50 dose of metformin was 57.3 µM for 24h in HepG2 cells. Metformin alone did not induce DNA damage at all studied concentrations (5-1000 µM) for 24h. However, at the concentration ranges between 5 µM and 1000 µM, it did not change H2O2-induced DNA strand breakage damage.

CONCLUSIONS:

In conclusion, our results suggest that metformin has no potential effect in increasing or decreasing the oxidative stress-related genotoxicity in HepG2 cells. More mechanistic studies should be required in order to get more clear results.

ACKNOWLEDGEMENTS:

This study is supported by Hacettepe University Scientific Research Projects Coordination Unit under Grant number THD - b2017 – 13153.

REFERENCES:

1. Olokoba AB, Obateru OA, et al., (2012). Type 2 diabetes mellitus: a review of current trends. Oman medical journal, 27(4), 269.
2. Kasznicki J, Sliwinska A, et al., (2014). Metformin in cancer prevention and therapy. Annals of translational medicine, 2(6).

P-542: EXPRESSIONS OF GST AND P53 IN HUMAN OVER TUMOR AND NON-TUMOR TISSUES

[1] Kaygin, P., [2] Erdem, A., [2] Simsek, GG.,[1] Oguztuzun, S., [3] Coban,T., [1] Barmaksiz, G.,[1] Hayat, B., [4] Kocdogan, AK., [5] Kilic, M., [1] Dirican, O.

[1]Kirikkale University, Faculty of Arts and Sciences, Department of Biology, Kirikkale, Turkey

[2]Kecioren Educational and Research Hospital, Department of Pathology, Ankara, Turkey

[3]Ankara University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

[4]Istanbul Gelisim University, Vocational School of Health Sevices, Patology Laboratory Techniques, Istanbul, Turkey

[5]Ankara University Vocational School of Health Services Department of Pharmacy Services, Ankara, Turkey

INTRODUCTION:

Type 2 diabetes is the most common form of diabetes. Metformin is a prescription drug commonly used for treating type 2 diabetes in adults and children (1). Metformin has been suggested to be responsible for anti-cancer activity via enhancing oxidative DNA damage under oxidative condition (2). However there are contradictory results in the literature. This study was aimed to evaluate the cytotoxic and genotoxic effects of metformin in human liver cancer (HepG2) cells.

MATERIALS AND METHODS:

The cytotoxicity of metformin (0.5-64 μM) was determined by Thiazolyl Blue Tetrazolium Blue (MTT) assay and its genotoxicity (5-1000 μM) was evaluated by alkaline comet assay in HepG2 cells treated with/ without H2O2. DNA damage was expressed as DNA tail intensity.

RESULTS:

The cell viability significantly decreased at the doses above 4 μM. The IC50 dose of metformin was 57.3 μM for 24h in HepG2 cells. Metformin alone did not induce DNA damage at all studied concentrations (5-1000 μM) for 24h. However, at the concentration ranges between 5 μM and 1000 μM, it did not change H2O2-induced DNA strand breakage damage.

CONCLUSIONS:

In conclusion, our results suggest that metformin has no potential effect in increasing or decreasing the oxidative stress-related genotoxicity in HepG2 cells. More mechanistic studies should be required in order to get more clear results.

ACKNOWLEDGEMENTS:

This study is supported by Hacettepe University Scientific Research Projects Coordination Unit under Grant number THD - b2017 – 13153.

REFERENCES:

1. Olokoba AB, Obateru OA, et al., (2012). Type 2 diabetes mellitus: a review of current trends. Oman medical journal, 27(4), 269.
2. Kasznicki J, Sliwinska A, et al., (2014). Metformin in cancer prevention and therapy. Annals of translational medicine, 2(6).

P-543: MITOCHONDRIAL GST KAPPA1 ISOENZYME PROTEIN EXPRESSION IN BLADDER CANCER

[1] Oguztuzun, S., [1] Kaygin, P., [2] Simsek, GG., [3] Kocdogan, AK., [4] Kilic, M., [5] Bulus, H., [6] Coban, T., [1] Dirican, O.

[1]Kirikkale University, Faculty of Arts and Sciences, Department of Biology, Kirikkale, Turkey

[2]Kecioren Educational and Research Hospital, Department of Pathology, Ankara, Turkey

[3]Istanbul Gelisim University, Vocational School of Health Sevices, Patology Laboratory Techniques, Istanbul, Turkey

4Ankara University Vocational School of Health Services Department of Pharmacy Services, Ankara, Turkey

5Keçiören Educational and Research Hospital, Department of Surgery, Ankara, Turkey

6Ankara University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

INTRODUCTIONS:

Glutathione S-Transferases (GSTs) are enzyme groups that biotransform several compounds known to be risk factors for urothelial carcinoma. By catalysis to the -SH group of the antioxidant glutathione, they protect normal cells from potentially harmful environmental substances such as carcinogens and xenobiotics (1,2). Detoxification of these compounds accelerates their dissolution in aqueous cells and their excretion from the body (3). GST enzyme system is important for drugs, enviromental pollution and carcinogen biotransformation. In this study, we investigated GST Kappa (K1) isoenzyme with immunohistochemical staining for possible effect on the patogenesis of bladder cancer.

MATERIALS AND METHODS:

For immunohistochemical studies, tissues were obtained from 49 patients with bladder carcinoma. GSTK1 expression in tumor and control tissues of patients was compared according to their staining intensity. Relationships between GSTK1 expressions

in tumor and control tissue were examined by the Mann Whitney-U test, and the clinicopathological data were examined by the Spearman correlation rank test.

RESULTS:

When the tissues of these cases were compared according to their staining intensity, GSTK1 expression in bladder carcinoma was significantly higher than normal bladder tissues (p=0,0000; 0,000<0,05). When the immunohistochemical result of GSTK1 isoenzyme was correlated with the clinical parameters, they were not correlated with age, gender, tumor stage, grade, smoking status, (p>0,05).

CONCLUSIONS:

According to these findings, it is likely to be of importance GSTK1 isozyme in the diagnosis of bladder cancer. In bladder cancer patients the higher expressions of GSTK1 proteins in tumor than normal bladder tissues might be important in papillary urothelial bladder cancer development.

REFERENCES:

1. Berendsen CL, Peters WH, et al., (1997). Glutathione S-transferase activity and subunit composition in transitional cell cancer and mucosa of the human bladder. Urology, 49, 644-51.
2. Cohen SM, Shirai T, et al., (2000). Epidemiology and Etiology of Premalignant and Malignant Urothelial Changes. Scand J Urol Nephrol, 34, 105-15.
3. Catto JW, Yates DR, et al., (2007). Behavior of urothelial carcinoma with respect to anatomical location. J Urol, 177, 1715-20.

P-544: IS THERE A NEGATIVE ASSOCIATION BETWEEN BORON EXPOSURE AND BIRTH WEIGHT OF NEWBORNS?

[1] Duydu, Y., [2] Basaran, N., [1] Ustundag, A., [2] Aydin, A., [3] Yalcin, CO., [2] Anlar, HG., [2] Bacanli, M., [4] Aydos, K., [4] Atabekoglu, CS., [5] Golka, K., [6] Ickstadt, K., [7] Schwerdtle, T., [7] Werner, M., [6] Meyer, S., [5] Bolt, HM.

[1]Ankara University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey.

[2]Hacettepe University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey.

[3]Karadeniz Technical University, Faculty of Pharmacy, Department of Toxicology, Trabzon, Turkey 4Ankara University, Faculty of Medicine, Ankara, Turkey.

5Leibniz Research Center for Working Environment and Human Factors (IfADo), Dortmund, Germany.

6Technical University (TU) Dortmund, Faculty of Statistics, Dortmund, Germany.

7University of Potsdam, Institute of Nutritional Science, Department of Food Chemistry, Nuthetal, Germany

INTRODUCTION:

Recently, a study group conducted a study in a boron exposed females in Northern Argentina and reported a negative association between high level of boron exposure and birth size (1). This is the only study that suggest a negative association between boron exposure and birth size so far. Therefore the results of this study should be clarified in a population exposed to high level of boron in daily life. The aim of the present study is to investigate the birth weight of newborns in a highly boron exposed population in Bandırma and Bigadiç in order to corroborate or refute the above reported association between birth weight of newborns and boron exposure.

MATERIALS AND METHODS:

The study protocols approved by the Ethics committee of the Ankara University School of Medicine (no: 20-853-14, date: 08.12.2014). The blood samples (n=199) were sampled from females residing in Bandırma and Bigadiç. Information on the birth weight of newborn was gathered by the questionnaire. Blood boron concentrations of the participated females were determined by using ICP-MS (Agilent 8800 ICP-QQQ) in the “no gas” mode. The females were classified into low, medium and high exposure groups according to their blood boron concentrations in order to investigate the boron mediated effects on birth weights of newborns.

RESULTS:

The mean blood boron concentrations of low, medium and high exposure groups were 39.74 ± 27.60, 124.19 ± 13.10 and 274.58 ± 213.00 ng B/g blood respectively. The mean blood boron concentrations of the medium and high exposure group were significantly higher ($p<0.05$) than the low exposure group. This result indicates to high level of boron exposure in medium and high exposure groups. The mean birthweights of newborns in low medium and high exposure groups were 3213.47 ± 560.67, 3082.81 ± 562.80 and 3112.42 ± 708.95 gram respectively. The pairwise difference in mean birthweights were statistically not significant ($p>0.05$)

CONCLUSIONS:

In spite of a high level of boron exposure, negative association between boron exposure and birth weights of newborns were not observed. Our results refute the negative association suggested by Igra et al (1) between boron exposure and birthweight of newborns.

ACKNOWLEDGEMENTS:

This study was supported by the Eti Mine Works General Management (2014-2017).

REFERENCES:

1. Igra AM, Harari F, et al., (2015). Environment International, 95:54-60.

P-545: Y:X SPERM RATIO IN MALE WORKERS EMPLOYED IN BORIC ACID PRODUCTION PLANT

[1] Yalcin, CO., [2] Ustundag, A., [2] Duydu, Y.

[1] Karadeniz Technical University, Faculty of Pharmacy, Department of Toxicology, Trabzon, Turkey

[2] Ankara University, Faculty of Pharmacy, Department of Toxicology, Ankara, Turkey

INTRODUCTION:

In 2008, Robbins et al reported an association between high level of boron exposure and decreased Y:X sperm ratio in mail workers employed in boron mines/processing plants in Kuandian City, China (1). The authors have reported a boron mediated decrease in Y:X sperm ratio in male workers (n=63). The results of this study, however, have been criticized by other authors due to many weaknesses of the study design (2). Nevertheless, it is still a matter of debate whether high level of boron exposure is leading to a decrease in Y:X sperm ratio in men. Our study is aimed to investigate Y:X sperm ratio in highly boron exposed male workers in order to corroborate or refute the above reported association between Y:X ratio and boron exposure.

MATERIALS AND METHODS:

The blood and semen samples were sampled and used in accordance with the study protocols approved by the Ethics committee of the Hacettepe University School of Medicine (no: HEK 08/167, date: 22.10.2008). The semen and blood samples were sampled from the Bandrma Boric Acid Production plant and its surrounding facilities. The total number of sampled blood and semen samples were 163 and 86 of them were belonging to the boron exposed group. Blood boron concentrations of the participated workers were determined by using ICP-MS with flow injection system. Y- or X- bearing sperm cells in semen samples were detected by using fluorescence in situ hybridization (FISH) technique. The "Cytocell FAST FISH prenatal X, Y and 18 Enumeration Probe Kit (LPF 002) was used in detection and quantification of chromosomes X, Y and 18 by FISH. The probes are specific for the alpha satellite DNA sequences at the DXZ1, DYZ3 and D18Z1 regions of the chromosome X (green), Y (orange) and 18 (blue) respectively.

RESULTS:

The mean blood boron concentrations in control and boron exposed male workers were 63.56 ± 43.89 (<LOQ – 252) and 141.55 ± 80.43 (25.20 – 454) ng B/g blood respectively. The significantly high level of blood boron concentrations ($p<0.05$) of exposed workers proved the high level of boron exposure in our study population. The Y:X sperm ratios in control and exposed group were determined as 0.99 ± 0.03 (0.85 – 1.10) and 0.99 ± 0.02 (0.86 – 1.04) respectively. The difference between control and exposed groups was statistically not significant ($\chi 2$ test, $p>0.05$).

CONCLUSIONS:

In spite of the high level of boron exposure boron mediated decrease in the Y:X sperm ratio was not determined in our study population. Our results refute the association suggested by Robbins et al between high level of boron exposure and decreased Y:X sperm ratio in men.

ACKNOWLEDGEMENTS:

This study was supported by BOREN (2008-G0207) and Ankara University BAP (14B0237004).

REFERENCES:

1. Robbins WA, Wei F, et al., (2008). Journal of Andrology, 29:115-121.
2. Scialli AR, Bonde JP, et al,. (2010). Reproductive Toxicology, 29:10-24.

P-546: MORPHINE DETECTION BY SURFACE ENHANCED RAMAN SPECTROSCOPY

[1] Akcan, R., [1] Yildirim, MS., [2] Ilhan, H., [3] Tamer, U., [3] Saglam, N.

[1]Hacettepe University, Medical Faculty, Department of Forensic Medicine, Ankara, Turkey

[2]Hacettepe University Department of Nanotechnology and Nanomedicine, Ankara, Turkey

[3]Gazi University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey

INTRODUCTION:

Introduction: Morphine is one of the most commonly abused drugs, and it can be detected by certain methods. Many toxicologists, forensic professionals still seek cheaper and faster ways to detect morphine. In this manner, Surface Enhanced Raman Spectroscopy (SERS) has many advantages over other methods. However, there are still controversies in the literature about SERS signature of morphine. This study aims to find out SERS spectra of morphine in order to set an alternative method.

MATERIALS AND METHODS:

Morphine, in acetonitrile solution, in concentration of 1 mg/mL was used as sample solution. Morphine solution was dropped as 2 µL on to Raman active Au surface. After an incubation period of five minutes, 2 µL of colloidal Ag nanoparticles was dropped on sample. Raman spectra gathered by a Raman Spectroscope with 785 nm laser source.

RESULTS:

Major peaks of morphine were determined as 534, 611, 630, 872 and 1348 s-1, respectively. Gathered spectra of morphine have been compared with those given in related literature.

CONCLUSIONS:

SERS spectra of morphine presented in the literature reflects Raman signature of morphine partially, compared to our study. Therefore presented method shows more accurate peaks with higher intensities when compared to related studies in the literature.

P-547: PHYSICAL COMPATIBILITY OF LOOP DIURETICS IN TOTAL PARENTERAL NUTRITION IN Y-SITE ADMINISTRATION

Tomczak SZ., Stawny M., Dettlaff K., Jelińska A.

Poznan University of Medical Sciences, Department of Pharmaceutical Chemistry, Poznań, Poland

INTRODUCTION:

Loop diuretics (e.g. furosemide and torsemide) are an effective drugs used in the treatment of hypertension in many regimens. In the case of patients on parenteral nutrition, a considerable challenge is posed by the need to combine pharmacotherapy and total parenteral nutrition (TPN). When the same venous access site is used for drug administration and for TPN, it is necessary to discontinue the infusion and cleanse the cannula. Before TPN is resumed, the venous access site must be cleansed again to prevent any unwanted interactions, such as sedimentation, stratification or discoloration, which may endanger the patient's health or life. For those reasons, Y-site drug delivery is a helpful solution that reduces the handling of the venous access site and thus the intervals between infusions, which improves patient nutrition. In any case, the co-administration of a drug and TPN may be considered only after completion of analytical tests performed to confirm that a particular drug-TPN combination is therapeutically safe.

The purpose of this study was to evaluate the physical compatibility of total parenteral nutrition and drugs in Y-site administration.

MATERIALS AND METHODS:

The compatibility of furosemide and torsemide with 6 TPN mixtures of different compositions based on Lipidem MCT/LCT emulsions was studied. Undiluted drugs were mixed 1:1 at ratios determined by infusion flow rates. Visual assessment was used to monitor the physical stability of the drugs and emulsions to detect any sedimentation, stratification and discoloration. In addition, the pH and osmolarity of the mixtures as well as the size of mixture particles were found. The study was conducted immediately after mixing (t =0h) and at 4 h.

RESULTS:

During the study no discoloration, stratification or sedimentation was observed. The pH and osmolarity of the mixtures did not change after 4 h of the experiment. The average particle size was 206,3-226,8 nm and satisfied requirements for parenteral emulsions (<500 nm).

CONCLUSIONS:

The study demonstrated the physical compatibility of furosemide and torsemide with TPN mixtures for Y-site administration. This indicates that the co-administration of furosemide and torsemide with TPN mixtures ensures therapeutic safety in the treatment of those patients with hypertension who require parenteral medication.

ACKNOWLEDGEMENTS

This study was supported by Poznan University of Medical Sciences grant of number 502-14-03305411-67212

P-548: THE INFLUENCE OF TPN MIXTURES COMPOSITION ON AMPICILLIN STABILITY

Stawny, M., Gostyńska A., Dettlaff, K., Jelińska A.

University of Medical Sciences, Department of Pharmaceutical Chemistry, Poznań, Poland

INTRODUCTION:

The stability of medicinal substances is an important element in the safety of pharmacotherapy. Administration to the patients' drugs without confirmed stability is a direct threat to their health and life. It is particularly important to confirm the possibility of co-administrate the medicinal product with other medicines or adding them to a medium not described in the SPC. A major problem in clinical practice is the use of intravenous pharmacotherapy in patients receiving total parenteral nutrition (TPN). TPN mixture is a compound drug resulting from the mixing at least 7 different solutions and lipid emulsion. Thus, it is very problematic to add other concomitant medications to such complex mixture. The aim of the study was to determine the possibility of adding ampicillin to TPN mixtures and to determine if content or type of any individual component of TPN affect the stability of this antibiotic.

MATERIALS AND METHODS:

The study material consisted of 2400 ml of TPN mixture (five different compositions) with the addition of 10 g ampicillin and the reference samples were prepared without addition of the drug. Studied mixtures were stored for 7 days at 5±1°C with light protection and analyzed each 24 hours. The content of the drug was determined by HPLC. At the same time, physical properties of the studied mixtures were evaluated: the pH (Mettler Toledo Seven Compact PH / ion S220®), the zeta potential and the lipid emulsion particle size (ZestaSizer Nano ZS).

RESULTS:

The highest stability of the oil-water system was found in the TPN mixtures containing the omega-3 fatty acids, whereas the lowest stability was observed

in TPN mixture with the increased amount of monovalent and divalent ions. Addtion of ampicillin to the TPN mixtures caused an increase in the pH value, small changes in the particle size of the lipid emulsion and a reduction in the zeta potential values. The degradation of ampicillin in the TPN mixtures occured according to the first order kinetics, and the rate of decomposition was dependent on the composition of the mixture and the storage conditions.

CONCLUSIONS:

Based on these results it can be concluded that the ampicillin did not cause changes in the physical properties of TPN mixtures. However, the obtained results indicate that ampicillin shows the highest stability in a high energy TPN mixture, and the lowest in the TPN with high electrolyte composition.

ACKNOWLEDGEMENTS

This study was supported by grant SONATA no. 2015/17/D/NZ7/00792 from the National Science Centre, Poland.

.

AUTHOR INDEX

Symbols

A

B

C

D

E

F

G

H

I

J

K

L

M

N

O

P

Q

R

S

T

U

V

W

Y

457

Z

LIST OF PARTICIPANTS

Name-Surname	e-mail	Country
Abbase Güleren AlsancaK	gulerenalsancak@sdu.edu.tr	Turkey
Abd El-Aty	abdelaty44@hotmail.com	Egypt
Abdullah Uslu		Turkey
Abdurrahman Aktümsek	aktumsek@selcuk.edu.tr	Turkey
Adam Matkowski	erasmus@mailplus.pl	Poland
Adnan Kadi	akadi@ksu.edu.sa	Saudı Arabıa
Adriano Mollica	a.mollica@unich.it	Italy
Afonso Miguel Navas Cavaco		Portugal
Ahmet Çağrı Karaburun	ackarabu@anadolu.edu.tr	Turkey
Ahmet Doğan Ergin	adergin@ankara.edu.tr	Turkey
Ahmet Oğuz Ada	ada@pharmacy.ankara.edu.tr	Turkey
Ahmet Özdemir	ahmeto@anadolu.edu.tr	Turkey
Ahsen Sevde Çınar	cinarahsen@gmail.com	Turkey
Aicha Kraimi		Algerıa
Aida Sapcanin	ida@bih.net.ba	Bosnıa And Herzegovına
Alaa Sami		Turkısh Republıc Of Northern Cyprus
Alessandra Gentili	alessandra.gentili@uniroma1.it	Italy
Alev Önder	pharmacogalev@gmail.com	Turkey
Alev Taşcıoğlu	alev.tascioglu@gmail.com	Turkey
Alexander Tropsha	alex_tropsha@unc.edu	Usa
Alf Lamprecht	alf.lamprecht@uni-bonn.de	Germany
Ali Erdinç Yalın	aeyalin@gmail.com	Turkey
Ali Ergüç	alierg33@gmail.com	Turkey
Ali Kemal Ateş	akates@ankara.edu.tr	Turkey
Ali Türkyılmaz		Turkey
Ali Yaprak	li.yaprak@hotmail.com	Turkey
Alija Uzunovic	alijauzunovic@gmail.com	Bosnıa And Herzegovına
Alpcan Eroğlu	alpcan9534@hotmail.com	Turkey
Alper Arslan	lprarsln@gmail.com	Turkey
Alper Çimik	a.cimik@hotmail.com	Turkey
Alper Gökbulut	gokbulut@pharmacy.ankara.edu.tr	Turkey
Alper Öztürk	aaozturk@anadolu.edu.tr	Turkey
Arben Merkoçi	arben.merkoci@icn2.cat	Spaın
Arın Gül Dal	agdal@anadolu.edu.tr	Turkey
Arif Cetin	arif.engin.cetin@gmail.com	Turkey
Arif Tanju Özçelikay	ozcelikay@ankara.edu.tr	Turkey
Arzu Beşikçi	abesikci@ankara.edu.tr	Turkey
Arzu Karakurt	arzu.karakurt@inonu.edu.tr	Turkey
Arzu Karayel	arzukarayel@hitit.edu.tr	Turkey
Arzu Özel	arzuozenozel@ktu.edu.tr	Turkey
Arzu Palandöken		Turkey
Arzu Zeynep Karabay	zeynepkarabay@yahoo.com	Turkey
Asaf Evrim Evren	asafevrimevren@anadolu.edu.tr	Turkey
Aslı Koç	aslikoc79@gmail.com	Turkey
Aslıhan Hilal Algan	eczaslihanhilal@yahoo.com	Turkey
Aslıhan Kubilay	akubilay@anadolu.edu.tr	Turkey
Asuman Bozkır	bozkir@pharmacy.ankara.edu.tr	Turkey
Aybala Temel	aybalatemel@hotmail.com	Turkey
Aybüke Çelik	celikaybke@gmail.com	Turkey
Aybüke Süveyda Boyraz	asboyraz@ankara.edu.tr	Turkey
Ayça Aktaş Şüküroğlu	aktasayca@hotmail.com	Turkey
Ayça Çakmak	ayca.cakmak@bozok.edu.tr	Turkey
Ayça Güngör	aycagungor93@gmail.com	Turkey
Ayça Mehmetoğlu	aycamehmetoglu@gmail.com	Turkey
Ayça Nur Türkoğlu		Turkey
Ayçe Çeliker	aycelike@hacettepe.edu.tr	Turkey
Aygin Bayraktar Ekincioğlu	aygin@hacettepe.edu.tr	Turkey

Name-Surname	e-mail	Country
Ayhan Savaşer	ayhan.savaser@sbu.edu.tr	Turkey
Ayhanım Elif Müderrisoğlu	muderrisoglu@ankara.edu.tr	Turkey
Aylin Atik		Turkey
Aylin Balcı	aylinbalci87@gmail.com	Turkey
Aylin Üstündağ	dur@pharmacy.ankara.edu.tr	Turkey
Aysel Koç Demir	akocaysel@yahoo.com	Turkey
Aysel Pehlivanlı	pehlivanli@ankara.edu.tr	Turkey
Aysu Merve Nalbur	aysumerve.nalbur@gmail.com	Turkey
Aysu Selçuk	aselcuk@pharmacy.ankara.edu.tr	Turkey
Aysun Geven	aysungeven@anadolu.edu.tr	Turkey
Aysun Ökçesiz	aysunokcesiz@gmail.com	Turkey
Ayşe Bozkurt	aysebozkurt300@hotmail.com	Turkey
Ayşe Didem Yılmaz	aysedidemyilmaz@mynet.com	Turkey
Ayşe Eken	eken.ayse@gmail.com	Turkey
Ayşe Ercan	ayseercan77@gmail.com	Turkey
Ayşe Gençer	aysegencer.11@gmail.com	Turkey
Ayşe Meltem Yalınay	meltemyc@gmail.com	Turkey
Ayşe Mine Gençler	gencler_65@yahoo.com	Turkey
Ayşe Nur Büke	bukeaysenur@gmail.com	Turkey
Ayşe Nur Oktay	aysenur-oktay@hotmail.com	Turkey
Ayşe Nur Yazgan	anyazgan@ankara.edu.tr	Turkey
Ayşe Nurten Özdemir	nozdemir@pharmacy.ankara.edu.tr	Turkey
Ayşegül Ateş		Turkey
Ayşegül Doğan	ayseguld@hacettepe.edu.tr	Turkey
Ayşegül İyidoğan	iyidogan@gantep.edu.tr	Turkey
Ayşegül Karataş	akaratas@pharmacy.ankara.edu.tr	Turkey
Ayşegül Köroğlu	aguvenc@ankara.edu.tr	Turkey
Aytekin Uzunoğlu	auzunoglu@konya.edu.tr	Turkey
Azeema Munir		Pakıstan
Aziz Baydar	a.baydar@ankara.edu.tr	Turkey
Azranur Dal	azranurdal@gmail.com	Turkey
Banu Kaşkatepe	bkaskatepe@ankara.edu.tr	Turkey
Banu Tel	banutel@hacettepe.edu.tr	Turkey
Başak Acar Karaköy		Turkey
Başak Özlem Perk	perk@ankara.edu.tr	Turkey
Bayram Kağan Akay	bayramkaganakay@gmail.com	Turkey
Bedia Koçyiğit Kaymakçıoğlu	bkaymakcioglu@marmara.edu.tr	Turkey
Bedriye Seda Kurşun Aktar	sedakursun@windowslive.com	Turkey
Begüm Evranos Aksöz	begumevranos@gmail.com	Turkey
Begüm Nurpelin Sağlık	bnsaglik@anadolu.edu.tr	Turkey
Belgin Sever	belginsever@anadolu.edu.tr	Turkey
Belma Gümüşel	belmagumusel@yahoo.com	Turkey
Belma Konuklugil	belma.konuklugil@gmail.com	Turkey
Benan Dursunoğlu	benan.dursunoglu@atauni.edu.tr	Turkey
Benay Can Eke	eke@pharmacy.ankara.edu.tr	Turkey
Bengi Uslu	buslu@pharmacy.ankara.edu.tr	Turkey
Bengi Uysaler	bengiuysaler@hacettepe.edu.tr	Turkey
Beril Altun	berilaltun@gmail.com	Turkey
Berin Karaman Mayack	bkaraman@biruni.edu.tr	Turkey
Berna Güven	bguven@ankara.edu.tr	Turkey
Berrin Küçüktürkmen	bbasaran@pharmacy.ankara.edu.tr	Turkey
Berrin Özbek		Turkey
Betül Arıca Yegin	byegin@yahoo.com	Turkey
Betül Buran		Turkey
Betül Kaya Çavuşoğlu	betulkaya@anadolu.edu.tr	Turkey
Betül Rabia Erdoğan	berdogan@ankara.edu.tr	Turkey
Betül Sever Yılmaz	sever@pharmacy.ankara.edu.tr	Turkey

Name-Surname	e-mail	Country
Bezhan Chankvetadze	jpba_bezhan@yahoo.com	Georgıa
Bilge Akcıl	bilgeakcil03@hotmail.com	Turkey
Bilge Sözen Şahne	bilgesozen@yahoo.com	Turkey
Bilgehan Doğru	bdogru@ankara.edu.tr	Turkey
Bilgen Başgut	bilgen.basgut@neu.edu.tr	Turkısh Republıc Of Northern Cyprus
Buket Aksu	buket.aksu@altinbas.edu.tr	Turkey
Buket Er Demirhan	erbuket@gmail.com	Turkey
Burak Bıyık	burakins@hotmail.com	Turkey
Burak Demirhan	burakdemirhan@hotmail.com	Turkey
Burak Temiz	burakttemiz@gmail.com	Turkey
Burcu Baba	burcu.baba@hotmail.com	Turkey
Burcu Devrim	burcuankara@hotmail.com	Turkey
Burcu Doğan Topal	doganb@ankara.edu.tr	Turkey
Burcu Kelleci Çakır	burcukey@yahoo.com	Turkey
Burcu Timur	burcutmr@gmail.com	Turkey
Burcu Ünlü Endirlik	burcuunlu@erciyes.edu.tr	Turkey
Burçin Ergene Öz	ergene@pharmacy.ankara.edu.tr	Turkey
Burçin Bozal Palabıyık	burcinbozal@hotmail.com	Turkey
Burçin Özüpek		Turkey
Bülent Gözcelioğlu	belma.konuklugil@gmail.com	Turkey
Bülent Kıran	kiran.bulent@gmail.com	Turkey
Bülent Özpolat	bozpolat@mdanderson.org	Usa
Büşra Arpaç	arpacbusra@gmail.com	Turkey
Büşra Cumhur	bcumhur@ankara.edu.tr	Turkey
Büşra Demir	ecz.busrademir@gmail.com	Turkey
Büşra Erdaş	bsrerdas@gmail.com	Turkey
Büşra Kandilli	busra.server@atauni.edu.tr	Turkey
Büşra Karpuz	busrakarpuz13@gmail.com	Turkey
Büşra Yaylacı	busrayaylaci@hotmail.com	Turkey
Can Ayan	can.ayann@gmail.com	Turkey
Can Tufan	eczcantufan@yahoo.com	Turkey
Canan Hasçicek	canan.ogan@pharmacy.ankara.edu.tr	Turkey
Canan Kuş	kus@pharmacy.ankara.edu.tr	Turkey
Cansel Köse Özkan	canselkose@gmail.com	Turkey
Cansu Kabasakal	cansukabasakal@gmail.com	Turkey
Cansu Uysal	cansuysal56@hotmail.com	Turkey
Carsten Ehrhardt	carsten.ehrhardt@tcd.ie	
Catapano Maria Carmen	catapanm@faf.cuni.cz	Czech Republıc
Cem Erkmen	cmrkmn@gmail.com	Turkey
Cemre Acar	cemre_001@hotmail.com	Turkey
Cennet Duran	durancennet@gmail.com	Turkey
Ceren Duraloğlu	cerdural@windowslive.com	Turkey
Ceren Özdemir		Turkey
Ceren Özkul	cerenozkul@hacettepe.edu.tr	Turkey
Ceren Yener	cerenynr180@hotmail.com	Turkey
Ceyda Afşin Berdanoğlu	ceydaafsinb@gmail.com	Turkey
Ceyda Sibel Kılıç	erdurak@pharmacy.ankara.edu.tr	Turkey
Ceyda Tuba Şengel Türk	ceyda.tugba.sengel@pharmacy.ankara.edu.tr	Turkey
Claudio Santi	claudio.santi@unipg.it	Italy
Çağla Efeoğlu	efeoglucagla@gmail.com	Turkey
Çağlar Macit	cmacit@medipol.edu.tr	Turkey
Çiğdem Akyürek		Turkey
Çiğdem Kanbeş Dindar	ckanbes@gmail.com	Turkey
Çiğdem Karaaslan	karaslan@pharmacy.ankara.edu.tr	Turkey
Çiğdem Karakoyun	cigdem.karakoyun@ege.edu.tr	Turkey
Çiğdem Sarıyıldız		Turkey
Çiğdem Yengin	emrah.kilinc@ege.edu.tr	Turkey

Name-Surname	e-mail	Country
Damla Kırcı	damlakirci@anadolu.edu.tr	Turkey
Daryono Hadi Tjahjono	daryonohadi@fa.itb.ac.id	Indonesıa
Demet Cansaran Duman	dcansaran@yahoo.com	Turkey
Demet Dayıoğlu	demet.dayioglu@outlook.com	Turkey
Demet Sinem Güden	dsinem.guden@gmail.com	Turkey
Demet Yılmaz	eczdemetylmz@gmail.com	Turkey
Deniz Kibar	dkibar@mersin.edu.tr	Turkey
Derya Bektaş	deryabektas11@gmail.com	Turkey
Derya Çiçek Polat	polatd@ankara.edu.tr	Turkey
Derya İlem Özdemir	deryailem@gmail.com	Turkey
Derya Osmaniye	dosmaniye@anadolu.edu.tr	Turkey
Didem Kart	dturk@hacettepe.edu.tr	Turkey
Didem Sema Geçgel	dgecgel@yahoo.com	Turkey
Didem Yılmaz Oral	didemyilmaz144@gmail.com	Turkey
Dilan Eker	dilan_eker@anadolu.edu.tr	Turkey
Dilay Kahvecioğlu	dilaykahvecioglu@hotmail.com	Turkey
Dilek Ak	dak@anadolu.edu.tr	Turkey
Dilek Battal	diakunal@yahoo.com	Turkey
Dilek Eskiköy Bayraktepe	dilekeskikoy@gmail.com	Turkey
Dilek Kul	dilekk@ktu.edu.tr	Turkey
Dilşat Arıksoysal	dilsat.ariksoysal@ege.edu.tr	Turkey
Diren Sarısaltık	dirensarisaltik@gmail.com	Turkey
Dolunay Merve Fakıoğlu	dolunaytopuz90@gmail.com	Turkey
Durişehvar Özer Ünal	durisehvar@gmail.com	Turkey
Duygu Altıparmak	duygusac@gmail.com	Turkey
Duygu Şimşek		Turkey
Duygu Yeniceli Uğur	dyeniceli@anadolu.edu.tr	Turkey
Duygu Yılmaz Usta	yilmazduyguusta@gazi.edu.tr	Turkey
Ebru Altuntas	ebru.altuntas@istanbul.edu.tr	Turkey
Ebru Arıoğlu İnan	arioglu@ankara.edu.tr	Turkey
Ebru Didem Coşar	ed.cosar@gmail.com	Turkey
Ebru Gökalp Özkorkmaz	ebrug76@gmail.com	Turkey
Ebru Zeytün	ebru.zytn2@gmail.com	Turkey
Ece Güler	ece__guler1@hotmail.com	Turkey
Ece Miser Salihoğlu	ecemiser@hotmail.com	Turkey
Ecem Kaya Sezginer	ecemkaya1989@gmail.com	Turkey
Eda Aydın Güldür	aydn_eda@yahoo.com.tr	Turkey
Eda Gökbulut		Turkey
Eda Mavioğlu	cgaliba@aliraif.com.tr	Turkey
Efe Baturhan Orman	efeorman@gmail.com	Turkey
Effionora Anwar	effionora.anwar@farmasi.ui.ac.id	Indonesıa
Ege Arzuk	egearzuk@gmail.com	Turkey
Egemen Şahin	egemensahin95@gmail.com	Turkey
Ekin Kurtul	ekurtul@ankara.edu.tr	Turkey
Ekrem Murat Gönülalan	emg@hacettepe.edu.tr	Turkey
Elçin Bakır	elcinozger@gmail.com	Turkey
Elçin Ezgi Ahi	eahi@gtu.edu.tr	Turkey
Elif Alançay	elif.alancay@gmail.com	Turkey
Elif Aras	eczelifaras@gmail.com	Turkey
Elif Aydos	elifaydos1811@gmail.com	Turkey
Elif Çalışkan Salihi	caliskanelif@gmail.com	Turkey
Elif Ertuna	elif.ertuna@gmail.com	Turkey
Elif Gizem Karaca	elifgizemkaraca@gmail.com	Turkey
Elif İnce	ecz.elifince@gmail.com	Turkey
Elif Seydim		Turkey
Elif Yaman	elif.yaman@bilecik.edu.tr	Turkey
Elmas Sarı	elmassarii@hotmail.com	Turkey

Name-Surname	e-mail	Country
Elvan Hasanoğlu Özkan	elvanelvan_06@hotmail.com	Turkey
Emel Öykü Çetin Uyanıkgil	emeloykucetin@yahoo.com	Turkey
Emine Elçin Emre	oruc@gantep.edu.tr	Turkey
Emine Şen	emine.sen@altinbas.edu.tr	Turkey
Emirhan Nemutlu	enemutlu@hacettepe.edu.tr	Turkey
Emre Fatih Bülbül	efbulbul@medipol.edu.tr	Turkey
Emre Kara	eczemrekara@outlook.com	Turkey
Emre Özgenç	emreozgenc90@gmail.com	Turkey
Emre Soydaş	emresoydas@gmail.com	Turkey
Emre Şefik Çağlar	escaglar@medipol.edu.tr	Turkey
Emre Uyar	eczemreuyar@hotmail.com	Turkey
Engin Koçak	kengin@hacettepe.edu.tr	Turkey
Erdal Dinç	dinc@ankara.edu.tr	Turkey
Erdem Büyükbingöl	ebuyukbingol@gmail.com	Turkey
Erem Bilensoy	eremino@hacettepe.edu.tr	Turkey
Eren Aytekin	erenaytekin@hacettepe.edu.tr	Turkey
Eren Uzunkay		Turkey
Erhan Tan	etanerciyes@gmail.com	Turkey
Erkan Azizoğlu	azizoglu.erkan@gmail.com	Turkey
Erkan Can Köse	erkancank@gmail.com	Turkey
Erol Şener	erolsener@anadolu.edu.tr	Turkey
Ertuğrul Keskin	ekeskin@adiyaman.edu.tr	Turkey
Erva Özkan	arvarita@gmail.com	Turkey
Esin Akı Yalçın		Turkey
Esin Aysel Kandemir	esaykandemir@gmail.com	Turkey
Esin Karataş	esin_chem@hotmail.com	Turkey
Esra Pezik	esra_pzk@hotmail.com	Turkey
Esra Saylak	saylakesra@hotmail.com	Turkey
Esra Yarış	esra.yaris@dicle.edu.tr	Turkey
Evrim Yenilmez	evrimakyil@anadolu.edu.tr	Turkey
Eyüp Can Polat	eyupcanpolat@yahoo.com.tr	Turkey
Ezgi Gülpınar	ezgi_gulpinar@hotmail.com	Turkey
Ezgi Kıvrak		Turkey
Ezgi Öztaş	ezgi.oztas@istanbul.edu.tr	Turkey
Fahriye Ulya Badıllı	unuman@pharmacy.ankara.edu.tr	Turkey
Faika Başoğlu	faika.basoglu1990@gmail.com	Turkey
Fatıma Doğanç	doganc@ankara.edu.tr	Turkey
Fatih Demirci	fdemirci@anadolu.edu.tr	Turkey
Fatih Elay		Turkey
Fatih Tok	fatih.tok@marmara.edu.tr	Turkey
Fatih Ürkmez	furkmez@ankara.edu.tr	Turkey
Fatma Ağın	fagin@ktu.edu.tr	Turkey
Fatma Ayaz	fatmaayaz88@hotmail.com	Turkey
Fatma Çakır		Turkey
Fatma Gülay Der		Turkey
Fatma Gülgün Ozansoy	ozansoy@ankara.edu.tr	Turkey
Fatma Memnune Eruçar	memnune.erucar@istanbul.edu.tr	Turkey
Fatma Nisa Ballı	nisaballi16@gmail.com	Turkey
Fatma Özge Gökmen	fatmaozge.gokmen@bilecik.edu.tr	Turkey
Fatma Özlem Kargın Solmaz	ozlemhayati@hotmail.com	Turkey
Fatma Tosun	ftosun@medipol.edu.tr	Turkey
Fatma Tuğçe Gürağaç	ecztugceguragac@gmail.com	Turkey
Fatmanur Tuğcu Demiröz	nurtugcu@yahoo.com	Turkey
Fawaz Katrji	fawaz.katerji@gmail.com	Turkey
Ferhat Farşi		Turkey
Fırat Salman		Turkey
Figen Onuk Gören		Turkey

Name-Surname	e-mail	Country
Fikret Yıldız		Turkey
Fikriye Zengin	fzengin@ankara.edu.tr	Turkey
Filiz Bakar Ateş	fbakar@ankara.edu.tr	Turkey
Filiz Taşpınar	lzozkaya@gmail.com	Turkey
Fulya Levent		Turkey
Fügen Aktan	fugenaktan@hotmail.com	Turkey
Füsun Acartürk	acarturk@gazi.edu.tr	Turkey
Gaia Colombo	clmgai@unife.it	Italy
Gamze Çamlık	gamzecamlik@gmail.com	Turkey
Gamze Ekici		Turkey
Gamze Rüzgar Özemre	gamzeruzgar@gazi.edu.tr	Turkey
Gamze Eroğlu	gamzeeroglu@ktu.edu.tr	Turkey
George Jibuti	giorgi.jibuti@tsu.ge	Georgıa
Gi□zem Gülpınar	gaykac@gmail.com	Turkey
Gizem Kaykı Mutlu	gkayki@ankara.edu.tr	Turkey
Gizem Özkemahlı	kubragizem89@hotmail.com	Turkey
Gizem Rüya Topal	camca@ankara.edu.tr	Turkey
Gizem Tırıs	gizem.tiris@gmail.com	Turkey
Golshan Zare	golshanzare@gmail.com	Turkey
Gökalp Çetin	gokalpcetin@hacettepe.edu.tr	Turkey
Gökay Albayrak	albayrakgokay@gmail.com	Turkey
Gökberk Bulmuş	eczgokberkbulmus@gmail.com	Turkey
Gökçe Cihan Üstündağ	gokcechn@istanbul.edu.tr	Turkey
Gökçe Öztürk	gokceozturk@ktu.edu.tr	Turkey
Gökçen Telli	gokcentelli@hacettepe.edu.tr	Turkey
Gökhan Köroğlu		
Gökhan Zengin	gokhanzengin@selcuk.edu.tr	Turkey
Göksu Özçelikay	goksu.ozcelikay91@gmail.com	Turkey
Göksu Yağ Çilingiroğlu		Turkey
Gözde Öztürk	g.ozturkau@gmail.com	Turkey
Gözde Yenice		Turkey
Gustavo A. Rivas	grivas@fcq.unc.edu.ar	Argentına
Gülbahar Özge Alim	g.ozgealim@gmail.com	Turkey
Gülbike Demirel	gulbikedemirel@gmail.com	Turkey
Gülbin Özçelikay	gozcelikay@ankara.edu.tr	Turkey
Gülderen Yılmaz	gyilmaz@ankara.edu.tr	Turkey
Gülgün Kılcıgil	kilcigil@pharmacy.ankara.edu.tr	Turkey
Gülin Amasya	gamasya@pharmacy.ankara.edu.tr	Turkey
Gülin Renda	gulingurhan@yahoo.com	Turkey
Gülnur Ekşi Bona	gulnur_eksi@yahoo.com	Turkey
Gülsel Yurtdaş Kırımlıoğlu	gyurtdas@anadolu.edu.tr	Turkey
Gülsen Bayrak	gulsenyilmaz61@gmail.com	Turkey
Gülsen Kendir	kendir80@hotmail.com	Turkey
Gülsüm Atasoy		Turkey
Gülsüm Hale Özmert Coşkun		Turkey
Gülsüm Yıldız	gulsumyildiz@anadolu.edu.tr	Turkey
Hafize Yuca	hafize.yuca@atauni.edu.tr	Turkey
Hakan Eroğlu	ehakan@hacettepe.edu.tr	Turkey
Hakan Göker	goker@ankara.edu.tr	Turkey
Halise Ebrar Hekimoğlu	hekimoglu2015@hotmail.com	Turkey
Hanan Fael	hfael@ku.edu.tr	Syrıa
Hande Aygün	ecz_hndaygun@hotmail.com	Turkey
Hande Büşra Keleş	handebusra@gmail.com	Turkey
Hande Durusöz	h_duru89@hotmail.com	Turkey
Hanif Shirinzadeh	hanif.shirinzade@gmail.com	Turkey
Harun Uslu	harun.uslu@inonu.edu.tr	Turkey
Hasan Aydın	haydin@adiyaman.edu.tr	Turkey

Name-Surname	e-mail	Country
Hasan İlhan	ilhanhasan81@gmail.com	Turkey
Hasret Subak	ecz.hasrets@gmail.com	Turkey
Hasya Nazlı Ekin	hasyaekin@gmail.com	Turkey
Hatice Gül Anlar	haticegulanlar@gmail.com	Turkey
Hatice Kaplan Can	hkaplan@hacettepe.edu.tr	Turkey
Hatice Kübra Zeybek	hkzeybek@ankara.edu.tr	Turkey
Hayati Çelik	hayaticelik@gmail.com	Turkey
Hayrettin Tonbul	hayrettintonbul@hotmail.com	Turkey
Hayrettin Tümtürk	tumturk@gazi.edu.tr	Turkey
Hayriye Eda Şatana Kara	eda@gazi.edu.tr	Turkey
Hayriye Gülçin Saltan İşcan	gulcin.saltan@pharmacy.ankara.edu.tr	Turkey
Hayriye İçin	hayriye.icin@abdiibrahim.com.tr	Turkey
Hayrünnisa Taşcı	hayrunnisa_tasci@hotmail.com	Turkey
Hazal Ezgi Gültekin		Turkey
Hazel Sipahi		Turkey
Hediye Kamuran İleri	kamuranileri@gmail.com	Turkey
Hilal Başak Erol	hcuhadaroglu@ankara.edu.tr	Turkey
Hilal Özbek	hilalozbek@yahoo.com	Turkey
Hilal Tosun	hilaltosun43@gmail.com	Turkey
Hisahiro Kai	hkai@phoenix.ac.jp	Japan
Hülya Ortak	hulya.yilmaz0006@gmail.com	Turkey
Hüseyin Onur Tuncay	onur.tuncay@istanbul.edu.tr	Turkey
Hüseyin Servi	huseyin.servi@altinbas.edu.tr	Turkey
Hüsniye Birnur Güzeldağ	birnurguzeldag@gmail.com	Turkey
Iman Al Gorane	eman.sheikhli@gmail.com	Turkey
Iryna Gavrylova	iryna.gavrylova@gmail.com	Ukraıne
Işıl Özakca	isilozakca@gmail.com	Turkey
Ivan Kosalec	ikosalec@pharma.hr	Croatıa
Iza Matarashvili	iza.matarashvili@gmail.com	Georgıa
İbrahim Seyda Uras	ibrahimseydauras@hotmail.com	Turkey
İffet İrem Çankaya	iremtatli@hacettepe.edu.tr	Turkey
İlay Sema Ünal	ilaysema@gmail.com	Turkey
İleyda Çelik		Turkey
İlkay Yıldız	ilkayyildiz48@gmail.com	Turkey
İlker Ateş	ilkerates976@gmail.com	Turkey
İnci Barut	incibarut@anadolu.edu.tr	Turkey
İnci Selin Doğan	selinci@gmail.com	Turkey
İncilay Süslü	isuslu@hacettepe.edu.tr	Turkey
İpar Coşkun Ünlütürk	iparcoskun@mn.com.tr	Turkey
İpek Erol	ipekerol@gmail.com	Turkey
İrem Aydın	iremaydin04@gmail.com	Turkey
İrem Bozbey	irembzby@gmail.com	Turkey
İrem Çavuşoğlu	iremcav@hotmail.com	Turkey
İrem Karaömerlioğlu	ikaraomerlioglu@ankara.edu.tr	Turkey
İrem Kaya	ikaya19.07@hotmail.com	Turkey
İrfan Akartaş	irfanakartas@gmail.com	Turkısh Republıc Of Northern Cyprus
İrfan Erkan		Turkey
İshak Erik	ishakerik@ktu.edu.tr	Turkey
İsmail Çelik	ismailcelik@erciyes.edu.tr	Turkey
İsmail Murat Palabıyık	mpala@pharmacy.ankara.edu.tr	Turkey
İsmail Tuncer Değim	tdegim@biruni.edu.tr	Turkey
İsmail Yalçın	yalcin@ankara.edu.tr	Turkey
İsmet Çok	ismetcok@gmail.com	Turkey
İzel Ezgi Topaloğlu	itopaloglu@ankara.edu.tr	Turkey
Jean Luc Balligand	jean-luc.balligand@uclouvain.be	Belgıum
Jerka Dumic	jdumic@gmail.com	Croatıa
John Mcanaw	john.mcanaw@nhs24.scot.nhs.uk	Unıted Kıngdom

Name-Surname	e-mail	Country
Jose Manuel Pingarron Carrazon	pingarro@quim.ucm.es	Spaın
Joseph T. Chunu	josephchunu@gmail.com	Turkısh Republıc Of Northern Cyprus
Jun Haginaka	haginaka@mukogawa-u.ac.jp	Japan
Junichi Tanaka	jtanaka@sci.u-ryukyu.ac.jp	Japan
Kaan Birgül	kaanbirgul93@gmail.com	Turkey
Kader Çömlekçi	kcömlekci@bieameilac.com.tr	Turkey
Kadir Aykaç	kadirr050@gmail.com	Turkey
Kadir Yazıcı		Turkey
Kadri Güleç	kadrigulec@gmail.com	Turkey
Kamer Tecen Yücel	kamertecen@hacettepe.edu.tr	Turkey
Karel Šmejkal	karel.mejkal@post.cz	Czech Republıc
Kartini	kartini@staff.ubaya.ac.id	Indonesıa
Katarzyna Dettlaff	dettlaff@ump.edu.pl	Poland
Kayhan Bolelli	bolelli@ankara.edu.tr	Turkey
Kerem Polat	kerem_hybt@hotmail.com	Turkey
Kerem Şentürk	eczkeremsenturk@hotmail.com	Turkey
Keriman Özadalı Sarı	kozadali@hacettepe.edu.tr	Turkey
Kevser Biberoğlu	kevser.biberoglu@gmail.com	Turkey
Kıvılcım Öztürk Atar	kivilcimozturk@gmail.com	Turkey
Kibar Demirhan	demirhan.9082@gmail.com	Turkey
Kousha Zakeri	kooshazakeri@gmail.com	
Ksehiia Zazhyhina		
Kubilay Varol	kubilaymehmetvarol@gmail.com	Turkey
Kübra Durgun	kubradurgn@gmail.com	Turkey
Kürşat Kaya	kkaya@adiyaman.edu.tr	Turkey
Lali Tchankvetadze	progresixxichankv@yahoo.com	Georgıa
Levent Canyurt		Turkey
Levent Öner	loner@hacettepe.edu.tr	Turkey
Leyla Karadurmuş	leylakrdrms@gmail.com	Turkey
Lia Bezhitashvili	bezhitashvililia@yahoo.com	Turkey
M. Nazlı Şencan	nazlisencan@gmail.com	Turkey
Maciej Stawny	mstawny@ump.edu.pl	Turkey
Mahmoud Abudayyak	abudayyak@ktu.edu.tr	Turkey
Mahmoud F. Elsebai	elsebai72@yahoo.com	Egypt
Maja Peraica	mperaica@imi.hr	Croatıa
Maksut Coşkun	mcoskun@ankara.edu.tr	Turkey
Malek Hassan	malekamhassan@yahoo.com	Turkey
Marie-Aleth Lacaille-Dubois	m-a.lacaille-dubois@u-bourgogne.fr	France
Marlia Singgih Wibowo		Indonesıa
Mayuri Napagoda	mayurinapagoda@yahoo.com	Srı Lanka
Mehlika Dilek Altıntop	mdaltintop@anadolu.edu.tr	Turkey
Mehmet Alp	malp@ankara.edu.tr	Turkey
Mehmet Barlas Uzun	mehmetbarlasuzun@gmail.com	Turkey
Mehmet Berköz	mehmet_berkoz@yahoo.com	Turkey
Mehmet Can Sezgin		Turkey
Mehmet Evren Okur	evrenokurecz@gmail.com	Turkey
Mehmet Gökhan Çağlayan	caglayangokhan@gmail.com	Turkey
Mehmet Gümüştaş	mgumustas@hotmail.com	Turkey
Mehmet Levent Altun	altun@pharmacy.ankara.edu.tr	Turkey
Mehmet Murat Kışla		Turkey
Mehmet Onur Aksoy	onuraksoi@gmail.com	Turkey
Mehmet Sina İçen	sina.icen@inonu.edu.tr	Turkey
Mehmet Taşpınar	mtaspinartr@gmail.com	Turkey
Mehmet Uçuk	persmehmet@yandex.ru	Turkey
Mehmet Uzun	uzuneczanesi@hotmail.com	Turkey
Mehtap Kara	mehtap.kara@istanbul.edu.tr	Turkey
Melda Bahap	melda_610@hotmail.com	Turkey

Name-Surname	e-mail	Country
Melek Karacaoğlu	mkaracaoglu@ankara.edu.tr	Turkey
Melek Kurtaran	melekkurtaran@hacettepe.edu.tr	Turkey
Melek Sirin Baymak	msbaymak@marmara.edu.tr	Turkey
Meliha Ekinci	meliha.ekinci@ege.edu.tr	Turkey
Melike Yüksel	mel_yuksel@yahoo.com	Turkey
Meltem Ceylan Ünlüsoy	munlusoy@pharmacy.ankara.edu.tr	Turkey
Meral Tunçbilek	tuncbile@pharmacy.ankara.edu.tr	Turkey
Meriam Elhouid	meriam.elhouid@gmail.com	Tunusıan
Mert İlhan	eczmertilhan@gmail.com	Turkey
Merve Asena Öncül	asenaoncul@gmail.com	Turkey
Merve Bacanlı	mervebacanli@gmail.com	Turkey
Merve Becit	mervebecit@hotmail.com	Turkey
Merve Çelik Tekeli	merve.clk.145@gmail.com	Turkey
Merve Dalkıran	merve.dalkiran@pharmactive.com.tr	Turkey
Merve Demirbügen	demirbugen@ankara.edu.tr	Turkey
Merve Ergül	mergulmerve@gmail.com	Turkey
Merve Eryılmaz	merve.eryilmaz@gazi.edu.tr	Turkey
Merve Eylül Kıymacı	pharmaeyll@gmail.com	Turkey
Merve İnci Çamçi	merveinci21@hotmail.com	Turkey
Merve Memişoğlu	mmemisoglu@biruni.edu.tr	Turkey
Merve Mercan	mervemercan93@hotmail.com	Turkısh Republıc Of Northern Cyprus
Merve Nenni	merve.ecz@gmail.com	Turkey
Merve Şensoy	algalbiotek@gmail.com	Turkey
Merve Zengin	merveozdagli@hacettepe.edu.tr	Turkey
Meryem Erol	eczacimeryem@gmail.com	Turkey
Metin Emrah Kartal	eczmetinkartal@gmail.com	Turkey
Metin Yıldırım	metinyildirim4@gmail.com	Turkey
Mimouni Fatima Zohra	mimouni2401@yahoo.fr	Algerıa
Mine Günay İçtüzer	eczgny@gmail.com	Turkey
Mine Uzun	minebdr@gmail.com	Turkey
Mine Zanbak	eczminez@gmail.com	Turkey
Miray Aslan	msevuktekin@ankara.edu.tr	Turkey
Miray İlhan	mgorgoz@ankara.edu.tr	Turkey
Mircan Gürsel		Turkey
Miyase Gözde Gündüz	miyasegunduz@yahoo.com	Turkey
Mohammed Ali Selo	selom@tcd.ie	Iraq
Mohammed Saad Naji Ali	mohammadalgoli0@gmail.com	Turkey
Muhammad Sohail Arshad	sohail_arshad79@yahoo.com	Pakıstan
Muhammad Uzair	muhammaduzair@bzu.edu.pk	Pakıstan
Muhammed İhsan Han	hanihsan@gmail.com	Turkey
Muhammed Mesud Hürkul	mhurkul@ankara.edu.tr	Turkey
Murat Kozanlı	mrtkznl@gmail.com	Turkey
Murat Oral	ecz.murat.oral@gmail.com	Turkey
Murat Yaman	murat.yaman@bilkent.edu.tr	Turkey
Murat Yiğit		Turkey
Mustafa Bahadır Kaymaz	kaymazbahadir@gmail.com	Turkey
Mustafa Çelebier	celebier@hacettepe.edu.tr	Turkey
Mustafa Emrah Kılınç	kilincemrah@hotmail.com	Turkey
Mustafa Ergül	m.ergul@yahoo.com.tr	Turkey
Mutlu Aytemir	mutlud@hacettepe.edu.tr	Turkey
Müge Kılıçarslan	muge.kilicarslan@pharmacy.ankara.edu.tr	Turkey
Müge Savaş	mugeesavas@gmail.com	Turkey
Müjde Eryılmaz	meryilmaz@ankara.edu.tr	Turkey
Mümtaz İşcan	iscan@pharmacy.ankara.edu.tr	Turkey
Nadıa Bounoua	bounoua_nadia@yahoo.fr	Algerıa
Nadir Yalçın	nadir.yalcin@hotmail.com	Turkey
Nadire Özenver	nadire@hacettepe.edu.tr	Turkey

Name-Surname	e-mail	Country
Nafız Öncü Can	nafizoc@anadolu.edu.tr	Turkey
Naile Merve Güven	nmguven@ankara.edu.tr	Turkey
Nailla Jiwa		Turkısh Republıc Of Northern Cyprus
Nalan Yılmaz	nalan_y@anadolu.edu.tr	Turkey
Narin Sadıkoğlu	origanum@hotmail.com	Turkey
Nazlı Erdoğar	nerdogar@gmail.com	Turkey
Nazlı Turan Yücel	nazlituran@anadolu.edu.tr	Turkey
Necla Kulabaş	necla.kulabas@marmara.edu.tr	Turkey
Necmiye Canacankatan	ncanacankatan@gmail.com	Turkey
Neda Taner	ntaner@medipol.edu.tr	Turkey
Nefise Özlen Şahin	nefisesahin@gmail.com	Turkey
Nesligül Özdemir	nesliozdmr@hotmail.com	Turkey
Neslihan Aksu	neslihany.aksu@gmail.com	Turkey
Neslihan Üstündağ Okur	neslihanustundag@yahoo.com	Turkey
Nesrin Hökenek	nesrinhokenek@gmail.com	Turkey
Neşe Başak Türkmen	nesebasak86@gmail.com	Turkey
Nevena Ivanović	nevenam@pharmacy.bg.ac.rs	Serbıa
Nevin Erk	erk@pharmay.ankara.edu.tr	Turkey
Neziha Yağmur Diker	yagmurkumser@gmail.com	Turkey
Nil Demir	nildemir94@gmail.com	Turkey
Nilay Aleyna Durmaz	nadurmaz97@gmail.com	Turkey
Nilay Tarhan	eczmirayarslan@gmail.com	Turkey
Nilgün Günden Göğer	ngoger@gazi.edu.tr	Turkey
Nilüfer Yüksel	bozkir@pharmacy.ankara.edu.tr	Turkey
Nur İlge Çinar	nurilgecinar@gmail.com	Turkey
Nuray Arı	ari@ankara.edu.tr	Turkey
Nurdan Yazıcı Bektaş	ecz.nurdanyazici@gmail.com	Turkey
Nurettin Abacıoğlu	nabaci@gazi.edu.tr	Turkey
Nurgül Karadaş Bakırhan	nurgulk44@gmail.com	Turkey
Nuri Özmen	nuri.ozmen@ankara.edu.tr	Turkey
Nursel Sürmelioğlu	nurselisci@gmail.com	Turkey
Nurten Altanlar	naltanlar@ankara.edu.tr	Turkey
Oğuz Söğüt	o_sogut@yahoo.com	Turkey
Oğuzhan Fırat	ogzhnfrt@gmail.com	Turkey
Okan Arıhan	okanarihan@gmail.com	Turkey
Okan Onar	okanonar@gmail.com	Turkey
Okhtay Mousavigajlar	okhtay.m@gmail.com	
Omar Horani		Turkısh Republıc Of Northern Cyprus
Ongun Mehmet Saka	omsaka@gmail.com	Turkey
Onur Aşar	onur.asar@servier.com	Turkey
Osman Karabudak		Turkey
Oya Bozdağ Dündar	bozdag@pharmacy.ankara.edu.tr	Turkey
Ozan Kaplan	kaplan.ozan@hotmail.com	Turkey
Ömer Faruk Bahçecioğlu	omerfb92@hotmail.com	Turkey
Öncü Usluer		Turkey
Özge Akkoyun Muhiddin		Turkey
Özge Cansın Zeki		Turkey
Özge Demir	demirozge_@hotmail.com	Turkey
Özge Eşim	gun@ankara.edu.tr	Turkey
Özge İnal	inal@pharmacy.ankara.edu.tr	Turkey
Özge Kılıçaslan	ozgeeebayram@gmail.com	Turkey
Özge Özçınar	ozge.ozcinar7@gmail.com	Turkey
Özge Ülker	oulker@pharmacy.ankara.edu.tr	Turkey
Özgecan Gül Hizal	ozgehizal@outlook.com	Turkey
Özgün Sayıner	osayiner@ankara.edu.tr	Turkey
Özgür Devrim Can	ozgurdt@anadolu.edu.tr	Turkey
Özgür Eşim	ozgur.esim@sbu.edu.tr	Turkey

Name-Surname	e-mail	Country
Özgür Karban		Turkey
Özgür Üstündağ	ustundag@pharmacy.ankara.edu.tr	Turkey
Özgür Yılmaz	yilmaz.ozgur@tubitak.gov.tr	Turkey
Özlem Akbal Dağıstan	eczoslem@gmail.com	Turkey
Özlem Bahadır Acıkara	obahadir@ankara.edu.tr	Turkey
Özlem Öztürk Ceylan	ozturkozlemm@gmail.com	Turkey
Özlem Palancı	ozlem69@windowslive.com	Turkey
Özlem Temiz Arpacı	temiz@pharmacy.ankara.edu.tr	Turkey
Özüm Öztürk	ozozturk@ankara.edu.tr	Turkey
Patrick Walsh	asymmetriccat@gmail.com	Usa
Pelin Şenel	senelpelin88@gmail.com	Turkey
Pelin Telkoparan Akıllar	pelinta@yiu.edu.tr	Turkey
Pervin Betül Tekiner Gülbaş	btekiner@pharmacy.ankara.edu.tr	Turkey
Pınar Aslaner		Turkey
Pınar Bakır	pinar.bakir55@gmail.com	Turkey
Pınar Kara Kadayıfçılar	pinar.kara@ege.edu.tr	Turkey
Pınar Kul	pkul@ankara.edu.tr	Turkey
Pınar Namlı Uyanık		Turkey
Pierre Kondiah	pierre.kondiah@wits.ac.za	South Afrıca
Rabia Akman		
Ramazan Akçan	akcanmd@hotmail.com	Turkey
Ramazan Ceylan	biyoram7@gmail.com	Turkey
Rana Arslan	rbeis@anadolu.edu.tr	Turkey
Ratih	ratih.ratih@tu-braunschweig.de	Germany
Recai İnam	rinam@gazi.edu.tr	Turkey
Rengin Reis	renginreis@gmail.com	Turkey
Reyhan Neslihan Gürsoy	ngursoy@hacettepe.edu.tr	Turkey
Rukiye Sevinç Özakar	rukiyeso@atauni.edu.tr	Turkey
Rusudan Kakava	rusudan.kakava@gmail.com	Georgıa
Saadet Dermiş	dermis@pharmacy.ankara.edu.tr	Turkey
Safa Gümüşok	safagumusok@gmail.com	Turkey
Safiye Akkın	akkinsafiye@gmail.com	Turkey
Sakine Atila Karaca	sakineatila@anadolu.edu.tr	Turkey
Salvatore Fanali	salvatore.fanali@cnr.it	Italy
Samet Belveren	bvrnsamet@mersin.edu.tr	Turkey
Samet Poyraz	s.poyraz88@gmail.com	Turkey
Saniye Özcan	saniyeozcan@anadolu.edu.tr	Turkey
Sarah Khamis	dskhamis@gmail.com	North Cyprus
Sebila Özdemir	sebilaozdemir@gmail.com	Turkey
Seçil Karahüseyin	secil.karahuseyin@istanbul.edu.tr	Turkey
Seçil Sarıkaya Aydın	secilsarikaya@gmail.com	Turkey
Seda Ateş		Turkey
Seda Fandaklı	sedaf_84@hotmail.com	Turkey
Seda İpek	ipekseda94@gmail.com	Turkey
Seda Nur Topkaya	sedanur6@gmail.com	Turkey
Seda Önder	onderseda91@gmail.com	Turkey
Seda Rençber	sedarencber@gmail.com	Turkey
Sedef Kır		Turkey
Sedenay Akbaş	sedenayakbas@gmail.com	Turkey
Sefa Gözcü	h.sefa.gozcu@gmail.com	Turkey
Selda Zengin Kurnalı	selda.zengin@nobel.com.tr	Turkey
Selen Duygu Çeçen	duygucecen94@gmail.com	Turkey
Selen Gürkan Alp	selengurkan@gmail.com	Turkey
Selenay Sadak		
Selim Gök		Turkey
Selin Işık	selin.isik@neu.edu.tr	Trnc
Selin Tufan	eczselintufan@gmail.com	Turkey

Name-Surname	e-mail	Country
Selin Yüksel	selins.dogan@gmail.com	Turkey
Selma Saraç Tarhan	sesarac@hacettepe.edu.tr	Turkey
Selma Şahin		Turkey
Selman Şabanoğlu	sabanoglu@ankara.edu.tr	Turkey
Sema Arısoy	sarisoy@ankara.edu.tr	Turkey
Sema Çalış	scalis@hacettepe.edu.tr	Turkey
Semra Altunterim	semraterim@hotmail.com	Turkey
Sena F. Sezen	senasezen@ktu.edu.tr	Turkey
Serap Arabacı Anul	seraparabaci@gmail.com	Turkey
Serap Durkut	durkut@science.ankara.edu.tr	Turkey
Serap Gür	serapgur@ankara.edu.tr	Turkey
Serap İpek Dingiş	ipekdingis@gmail.com	Turkey
Serap Şahin Bölükbaşı	wserap@yahoo.com	Turkey
Serap Yalın	syalin01@hotmail.com	Turkey
Serap Yılmaz		Turkey
Sercan Baran	sercanbaran58@icloud.com	Turkey
Serdar Çetinkaya	serdarctnkaya@gmail.com	Turkey
Serdar Demir	serdar.demir@ege.edu.tr	Turkey
Serdar Tort	serdartort@gmail.com	Turkey
Serhat Sevgi	serhat_svg@hotmail.com	Turkey
Serkan Levent	serkanlevent@anadolu.edu.tr	Turkey
Serkan Özbilgin	ozbilgin@pharmacy.ankara.edu.tr	Turkey
Serkan Yiğitkan	syigitkan@hotmail.com	Turkey
Setyo Nurwaini	setyo.nurwaini@ums.ac.id	Indonesıa
Seval Olğaç	sevalolgac94@gmail.com	Turkey
Sevda Aydar	sevda.aydar@gmail.com	Turkey
Sevda Şenel	ssenel@hacettepe.edu.tr	Turkey
Sevda Türk	sevdaturk61@gmail.com	Turkey
Sevgi Şar	sevgisar98@gmail.com	Turkey
Sevgi Takka	takka@gazi.edu.tr	Turkey
Sevgi Yardım Akaydın	syakaydi@hotmail.com	Turkey
Sevil Şenkardeş	sevil.aydin@marmara.edu.tr	Turkey
Sevinç Kurbanoğlu	skurbanoglu@gmail.com	Turkey
Sevinç Şahbaz	sevren@marmara.edu.tr	Turkey
Seyhan Şahan Fırat	seyhansahan@mersin.edu.tr	Turkey
Sezen Yılmaz Sarıaltın	sezen.yilmaz@ankara.edu.tr	Turkey
Sezin Mert		Turkey
Shabuddin Memon	shahabuddinmemon@yahoo.com	Pakıstan
Shan Khazei	shankhazei1373@gmail.com	Turkey
Sıla Gülbağ	silagulbag@hotmail.com	Turkey
Sibel A. Özkan	ozkan@pharmacy.ankara.edu.tr	Turkey
Sibel Avunduk	sibelavunduk@mu.edu.tr	Turkey
Sibel Bozdağ Pehlivan	sbozdag@hacettepe.edu.tr	Turkey
Sibel İlbasmış Tamer	ilbasm@yahoo.com	Turkey
Sibel Süzen	sibel@pharmacy.ankara.edu.tr	Turkey
Sidar Bereketoğlu	sbereketoglu@ankara.edu.tr	Turkey
Sima Durmazpınar	simadurmazpinar@gmail.com	Turkey
Simla Olğaç	csimla@yahoo.com	Turkey
Sinan Süzen	suzen@pharmacy.ankara.edu.tr	Turkey
Sinem Aslan Erdem	saslan@pharmacy.ankara.edu.tr	Turkey
Sinem Saar	sinem.saar@gmail.com	Turkey
Slavica Razic	slavica.razic@pharmacy.bg.ac.rs	Serbıa
Slawomira Skrzypek	slawomira.skrzypek@chemia.uni.lodz.pl	Poland
Soner Alboy		Turkey
Suat Sarı	suat.sari@hacettepe.edu.tr	Turkey
Sulhiye Yıldız	suyildiz@ankara.edu.tr	Turkey
Sultan Pekacar	sultanpkcr94@gmail.com	Turkey

Name-Surname	e-mail	Country
Sumru Sözer Karadağlı	sozersumru@yahoo.com	Turkey
Suna Sibel Gürpınar	ssgurpinar@ankara.edu.tr	Turkey
Süleyman Aydın	saydin@anadolu.edu.tr	Turkey
Süleyman Kayan	eczkayan@hotmail.com	Turkey
Sülünay Parlar	sulunay.parlar@ege.edu.tr	Turkey
Sümeyra Tuna Yıldırım	stuna@erzincan.edu.tr	Turkey
Sümeyye Çoban	smeyyecoban@gmail.com	Turkey
Sündüz Alemdar	nurselbayramgil@gmail.com	Turkey
Şebnem Sarışan	sebnem.sarisan@abdiibrahim.com.tr	Turkey
Şefika Pınar Küçükkavruk	pnr.snl@hotmail.com	Turkey
Şirin Uysal	sirin.uysal@gmail.com	Turkey
Şule Dinç Zor	sule_dinc@yahoo.com	Turkey
Şura Baykan	sura.baykan@ege.edu.tr	Turkey
Şükran Öztürk	sukranozturk79@gmail.com	Turkey
Tahir Emre Yalçın	tahiremreyalcin@gmail.com	Turkey
Tamara Bakic	tbakic@pharmacy.bg.ac.rs	Serbıa
Tangül Şen	kilinc@pharmacy.ankara.edu.tr	Turkey
Tansel Çomoğlu	comoglu@pharmacy.ankara.edu.tr	Turkey
Taylan Turan	taylanturan35@gmail.com	Turkey
Tayyibe Beyza Yücel	beyza.cansu@gmail.com	Turkey
Thomas Olivier	olivier.thomas@nuigalway.ie	Ireland
Timuçin Uğurlu		Turkey
Tuba İnceçayır	tubaincecayir@hotmail.com	Turkey
Tuba Reçber	tuba.recber@hacettepe.edu.tr	Turkey
Tuba Taşkan	tubaataskan@gmail.com	Turkey
Tugrul Cagri Akman	eczcagri87@gmail.com	Turkey
Tuğba Adak	adaktuba@hotmail.com	Turkey
Tuğba Çopur	tugba-copur@hotmail.com	Turkey
Tuğba Eren Böncü	ecz.tugbaeren@gmail.com	Turkey
Tuğba Ertan Bolelli	tbolelli@ankara.edu.tr	Turkey
Tuğba Günbatan	tugbagunbatan86@yahoo.com	Turkey
Tuğbagül Çal	tgcal89@gmail.com	Turkey
Tuğçe Çapan	tugcecapan@gmail.com	Turkey
Tuğçe Demiröz	demirozt@hotmail.com	Turkey
Tuğçe Öğüt	tugceogut.94@gmail.com	Turkey
Tuğçe Özyazıcı	tugceozyazici90@gmail.com	Turkey
Tuğrul Mert Serim	serim@pharmacy.ankara.edu.tr	Turkey
Tunca Gül Altuntaş	altuntas@pharmacy.ankara.edu.tr	Turkey
Tutku Ceren Karabulut	tutkuceren.tck@gmail.com	Turkey
Tülay Çoban	coban@pharmacy.ankara.edu.tr	Turkey
Ufuk İnce	ecz.ufuk.ince@gmail.com	Turkey
Ugochukwu Chukwunyere	ugochux90@gmail.com	North Cyprus
Uğur Tamer	utamer33@yahoo.com	Turkey
Ukde Payze	ukdepayze@hotmail.com	Turkey
Ulviye Acar Çevik	uacar@anadolu.edu.tr	Turkey
Umay Merve Güven	umaymerveguven@gmail.com	Turkey
Umut Can Öz	umutcanoz@ankara.edu.tr	Turkey
Umut İrfan Üçel	uiucel@anadolu.edu.tr	Turkey
Ural Ufuk Demirel	ural.demirel@altinbas.edu.tr	Turkey
Ümide Demir Özkay	udemir@anadolu.edu.tr	Turkey
Ümmühan Kandemir	ummuhan_kandemir@hotmail.com	Turkey
Ümran Albuz		Turkey
Üzeyir Doğan	doganuzeyir@gmail.com	Turkey
Vahap Murat Kutluay	muratkutluay@hacettepe.edu.tr	Turkey
Veselina Adımcılar	adimcilar@itu.edu.tr	Turkey
Vesna Matovic	vesna.matovic@pharmacy.bg.ac.rs	Serbıa
Vildan Yozgatlı	vildanyozgatli@gmail.com	Turkey

Name-Surname	e-mail	Country
Vincent C.o. Njar	vnjar@som.umaryland.edu	Usa
Wafa Al-Jamal		Unıted Kıngdom
Wahyu Utami	wahyu.utami@ums.ac.id	Turkey
Wan Mohd Azizi Bin Wan Sulaiman	drwanazizi@iium.edu.my	Malaysıa
Y. Murat Elçin	elcin@ankara.edu.tr	Turkey
Yağmur Kılıçdağı	yagmursfl89@hotmail.com	Turkey
Yağmur Pirinçci	yagmur.pirincci@gmail.com	Turkey
Yahdiana Harahap	yahdiana03@yahoo.com	Indonesıa
Yalçın Duydu	duydu@pharmacy.ankara.edu.tr	Turkey
Yalçın Eroğlu	yeroglu24@hotmail.com	Turkey
Yalçın Özkan	yalcin.ozkan@sbu.edu.tr	Turkey
Yavuz Selim Çakmak	yavuzselimcakmak@gmail.com	Turkey
Yeşim Aktaş	yaktas@erciyes.edu.tr	Turkey
Yıldız Özalp		Turkısh Republıc Of Northern Cyprus
Yusuf Mülazim	yusuf.mulazim@neu.edu.tr	Turkey
Yusuf Özkay	yozkay@anadolu.edu.tr	Turkey
Zehra Ceren Ertekin	certekin@ankara.edu.tr	Turkey
Zehra Yazan		Turkey
Zekiye Ceren Arıtuluk	cerenarituluk@hotmail.com	Turkey
Zeliha Büyükbingöl	zbuyukbingol@ankara.edu.tr	Turkey
Zelihagül Değim		Turkey
Zerrin Sezgin Bayındır	zsezgin@pharmacy.ankara.edu.tr	Turkey
Zeynep Ateş Alagöz	zates@pharmacy.ankara.edu.tr	Turkey
Zeynep Doğan	zeynep.ocak2@gmail.com	Turkey
Zeynep Kalaycıoğlu	kalayciogluz@itu.edu.tr	Turkey
Zeynep Şafak Teksin	zsteksin@gazi.edu.tr	Turkey
Zeynep Ülkü Gün		Turkey
Zia Ur Rahman	ziaurrahman0938@gmail.com	Turkey
Zühal Güvenalp	guvenalp@atauni.edu.tr	Turkey
Zühal Kılıç Kurt	zkurt@ankara.edu.tr	Turkey

1975 YILINDAN BERİ
İNSAN SAĞLIĞINA DUYDUĞUMUZ
SAYGI
İLE HİZMET EDİYORUZ...

drogsan

Sağlığa Saygı

www.drogsan.com.tr

www.facebook.com/drogsanilaclari

www.twitter.com/drogsanilaclari

ISOPS-12 IS SUPPORTED BY TUBITAK
(The Scientific and Tecnological Research Council of Turkey)
with 2223-B Program)