ISOPS 14th International SYMPOSIUM ON PHARMACEUTICAL SCIENCES

TÜBİTAK
ISOPS14 is supported within the scope of
TÜBİTAK BİDEP 2223-B Grant Program

REPUBLIC OF TÜRKİYE
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TİKA

JUNE 25-28, 2024
ANKARA, TÜRKİYE

BOOK OF ABSTRACT

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Dear Participants and Guests,

I would like to express my sincere appreciation for the valuable contributions of all the participants of 14th International Symposium on Pharmaceutical Sciences (ISOPS). ISOPS, initiated in 1989, has been successfully brought international scientists, researchers, and students together from pharmaceutical sciences and related areas. This symposium was organized biannually until 1997 and then every three years.

Ankara University, Faculty of Pharmacy is the first faculty of pharmacy in Turkey and was established in 1960. Since the establishment, the institution rapidly progressed and now has very advanced scientific and physical infrastructure. Pharmaceutical science refers to a category of scientific fields and has followed important development processes, mainly in line with the developments in Biotechnology, Nanotechnology and Health Technologies, which are among the priorities of the technology fields of today. While realizing the modern requirements, our Faculty has a 5-year undergraduate education programme since 2005 and besides Turkish; it provides an English language of instruction programme since 2015. Our faculty has 7228 graduates since the established and the current number of students is 1267. Present educational and scientific resources allow a total of 112 faculty members, 48 professors, 25 associate professors, 7 assistant professors, 32 research assistants in our faculty. As of this year, we have a total of 1.177 undergraduate students, 789 in Turkish and 388 in English programs. Moreover, 58 administrative staff members and other personnel are working at different offices.

The mission of 14th 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 the most recent advances were discussed interactively and empowered the knowledge-based drug research development and multidisciplinary collaborations. It was our intention to make this symposium a memorable event.

This year, scientists from 22 countries were registered to ISOPS-14. Our programme consisted of 41 plenary, 132 oral and 192 poster presentations. Excellent research works were presented in different sessions. The speakers in the programme were uniquely placed in accordance with their area of expertise.

I would like to refer also to other initiatives that took place in our symposium. A workshop on "Innovative Health Technologies in Pharmacy Education" was held with the contribution of Prof. Lilian M. Azzopardi, Prof. Andrew Westwell, Prof. Zuriyadda Sakipova, Prof. Şule Apikoğlu, Assoc. Prof. Aysu Selçuk and Asst. Prof. Belma Pehlivanović Kelle. This workshop was interesting in terms of discussing the priorities and developments on this topic from local, regional and international respects.

On June 28, our panel on "Innovative Drugs from the Perspective of University-Industry and Public" was carried out by Prof. Dr. Asuman Bozkır. The heads and senior representatives of relevant institutions including; Assoc. Prof. Mehmet Kürşat Derici, Pharm. Dr. Elif İnci Ergönül, Pharm. Dr. Nihan Burul Bozkurt, Assoc. Prof. Hilal Yazıcı Malkoçoğlu, Prof. Dr. Erden Banoğlu, Prof. Dr. Hakan Akbulut, Prof. Dr. Zafer Çalışkan, Dr. Nadir Ulu and Dr. Ali Özüer were with us. This event has been a great platform to discuss the existing practices, requirements and propose solutions.

On behalf of the Organizing Committee, I would like to express my gratitude to the President of Ankara University who gave full support to the Symposium Organization. ISOPS-14 was organized successfully, without any professional support, with the dedication and contribution of all our faculty members, especially our symposium secretary Prof. Dr. Ceyda Tuba Şengel-Türk. I congratulate the organizing committee and all the other committees with all my heart and all academic and managing personnel because of their extensive work.

Prof. Dr. Asuman BOZKIR
Chair of ISOPS-14

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PLENARY LECTURES

PL01
DRUG DELIVERY STRATEGIES TO COMBAT AGE-RELATED SIGHT LOSS: A NEW ERA IN OPHTHALMIC THERAPEUTICS

Raid G.M. ALANY

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In the rapidly evolving field of ophthalmology, age-related sight loss has emerged as a significant challenge, mainly due to obstacles in the delivery of drugs and biologics to the front and back of the eye, a topic that will be the focus of Professor Raid Alany's plenary speech at the upcoming ISOPS-14 conference, titled "Drug Delivery Strategies to Combat Age-Related Sight Loss.

The presentation will explore the latest advancements in drug delivery strategies, focusing on the development of **polymeric inserts**, **microemulsions**, **in situ gelling systems, scaffolds, niosomes and nanoparticles**. These innovative systems have shown promise in enhancing the effectiveness of treatments for conditions such as age-related macular degeneration, diabetic retinopathy, dry eye, glaucoma, corneal wound healing, and diabetic keratopathies.

Professor Alany will discuss the hurdles associated with the use of various drugs and biologics, including **Ciclosporin**, **Timolol**, **Fasudil, Fenofibrate, Naltrexone and Connexin-43 antisense** in these delivery systems. The presentation will provide insights into how these drugs can be effectively formulated to treat the aforementioned ocular conditions.

The speech aims to not only present the current state of formulation and drug research undertaken by Professor Alany and his group but also stimulate further innovation in the field. Attendees can expect to gain a deeper understanding of the challenges and opportunities in developing effective treatments for age-related sight loss.

PL02
METALS LEVELS IN THE URINE OF ELECTRONIC CIGARETTE AND IQOS SMOKERS

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The use of electronic cigarettes (e-cigarettes) and heated tobacco products (IQOS) is increasing day by day in the world and in our country. There is no scientific evidence for the safety of e-cigarettes and IQOS, which are widely used especially among young people. In this study, it was aimed to compare heavy metal and nicotine exposures of e-cigarette users, IQOS users and smokers. A total of 117 volunteers, including IQOS, e-cigarette, smokers and non-smokers participated in the study. The levels of lead, cadmium, nickel, zinc and selenium metals to which the participants were exposed were determined and compared.

Lead level was 1,38±3,55 ng/g creatinine, 8,51±11,16 ng/g creatinine, 3,67±5,68 ng/g creatinine, 1,55 ±1,93 ng/g creatinine in e-cigarette, IQOS, smokers and control groups, respectively. Cadmium level was 0.22±0.22 ng/g creatinine, 0.28±0.33 ng/g creatinine, 0.48 ±0.64 ng/g creatinine, 0.35±0.34 ng/g creatinine in e-cigarette, IQOS, smokers and control groups, respectively. Nickel level was 3.43±2.16 ng/g creatinine, 3.85±4.11 ng/g creatinine, 1±1.42 ng/g creatinine 1.11±1.22 ng/g creatinine in e-cigarette, IQOS, smokers and control groups, respectively. Selenium level was 24.81±15.68 ng/g creatinine 27.75±22.02 ng/g creatinine, 26.01±18.10 ng/g creatinine, 22.98±21.06 ng/g creatinine in e-cigarette, IQOS, smokers and control groups, respectively. Zinc level was 298,40 ±221.78 ng/g creatinine and 596.13±779.14 ng/g creatinine, 217.59±142.75 ng/g creatinine, 285.03±233.34 ng/g creatinine in e-cigarette, IQOS, smokers and control groups, respectively. According to the data we obtained we obtained in our study, the lead level was found to be higher in the IQOS and smoking group, the cadmium level in the cigarette group, and the nickel level in the e-cigarette and IQOS user group compared to the other groups.

Key Words: E-Cigarette, Heavy Metals, IQOS

PL03
THE ACADEMIA-CRO TANDEM: THE DRUG DISCOVERY ENGINE OF THE FUTURE ?

Luc Van Hijfte

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The Pharmaceutical Industry has known a considerable drop in output of new drugs the last decades, and has been seeking solutions to tackle this issue. Following the megamergers and novel technology developments, there is currently a transformation ongoing of the Pharma R&D value chain. Large Pharma is aiming to share risks and costs, improve resource allocation and install a leaner, more agile R&D ecosystem based on open innovation concepts. The earlier phases of the drug discovery process are today more and more in the hands of biotech, academia and CRO's, funded by VCs, where then the large pharma will recover the assets at a later discovery stage to bring them to the market. This transformation, and an example of a collaboration between Oslo University and Symeres in the field of Tankyrase inhibitors, will be highlighted

From ChemMedChem 2023, Amjad A. et all.

Perspective doi.org/10.1002/cmdc.202300127

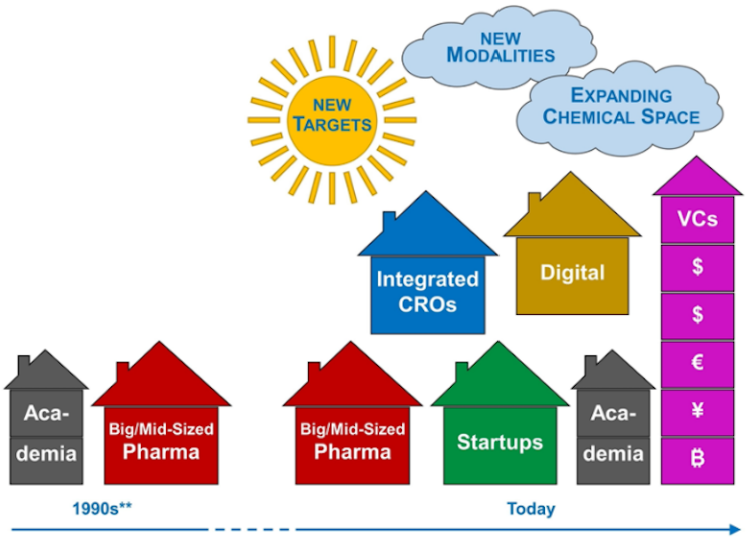

Figure 4. Exciting new science drives the evolving Pharma R&D Ecosystem. CRO = contract research organization. VC = venture capital (enterprises).[1]

PL04
MICROBIOLOGICAL CONTAMINATION OF MEDICINAL CANNABIS (CANNABIS SATIVA FLOWERING TOPS) – CURRENT STATUS.

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The use of the female parts of cannabis flowers, which are rich in cannabinoids, has a long tradition. Primarily, the collected and dried inflorescences, known as marijuana, are used for smoking or vaporising. Some member states of the European Union have legalised marijuana for personal use with certain restrictions. However, in the last two decades, cannabinoids in different chemotypes of *Cannabis sativa* L. with varying THC/CBD have attracted the attention of the scientific community, mainly because of their pharmacological effects on various health conditions and indications. As far as cannabis preparations in the EU are concerned, there are major differences between Member States. In some states, medical products containing cannabinoids are on the market as medicinal products with full marketing authorisation, in others there are oil-based medicinal products and still others offer a magistral prescription of cannabis flowers. Due to the different regulatory practises, all these medicinal products are only available in pharmacies with a doctor's prescription. In this presentation, we will focus on the quality requirements and/or recommendations for the female inflorescences of *Cannabis sativa* L. (Cannabis flos), which are used medicinally throughout Europe. As cannabis flowers are used for smoking as a "joint", vaporising (with a device) or with a rapid-onset delivery system, this route of administration may have adverse health effects due to the impurities contained in the cannabis flowers. Based on a bibliographic analysis and bibliometric review, we will present the current state of affairs regarding contamination issues related to different sources, including microbiological contamination, mycotoxin and heavy metals-related contamination. Based on guidelines for the cultivation and quality requirements of herbal medicines as well as pharmacopoeial recommendations for the control and limitation of contaminants, the special status of cannabis flowers when administered via the lungs will be discussed.

PL05
BLOOD-BRAIN BARRIER CULTURE MODELS TO PREDICT DRUG TRANSPORT TO THE BRAIN

Porkoláb, G., Szecskó, A., Vigh, JP., Gróf, I., Hoyk, Z., Walter, FR., Mészáros, M., Veszelka, S., Deli, MA.

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Introduction: The blood-brain barrier (BBB) hinders drug delivery to the brain and is implicated in neurological diseases. To better understand these processes in humans, there is a need for culture models that mimic the complexity of the BBB. However, state-of-the-art human BBB models either suffer from a non-physiological, mixed epithelial-endothelial identity or have weak barrier tightness, which greatly limits their usability. Our aim was to create an approach to improve the properties of BBB culture models that can be easily adapted.

Materials and Methods: Culture of human stem cell-derived endothelial cells, impedance-based measurement of barrier integrity, construction of the human endothelial cell and brain pericyte co-culture model, the measurement of transendothelial electrical resistance, tracer permeability, immunocytochemistry and image analysis, 3' RNA-sequencing and bioinformatic analysis, measurement of efflux pump activity, penetration of small molecule drugs across the human BBB model, synthesis and penetration of nanoparticles across the human BBB model, and statistics are described in our paper (1).

Results: We discovered that targeting three signaling pathways simultaneously, activation of cyclic AMP and Wnt/β-catenin signaling, and inhibition of the TGF-β pathway, in endothelial cells robustly induce BBB properties in vitro. To target this novel interaction, we identified a small molecule cocktail named cARLA, which synergistically enhanced barrier tightness in a range of BBB models across species. The three pathways converged on Wnt/β-catenin signaling to mediate the effect of cARLA via the tight junction protein claudin-5. The gene expressional profile of human stem cell-derived endothelial cells was shifted towards the in vivo brain endothelial signature, with a higher efflux pump activity and lower rates of endocytosis. Most importantly, cARLA improved the predictive value of the human BBB model regarding the brain penetration of a set of 10 small molecular drugs and glutathion-targeted nanoparticles.

Conclusions: The molecule combination has the potential to improve BBB culture models across laboratories to advance both basic research and drug development for the human brain.

Acknowledgements: This study was supported by grants from the National Research, Development and Innovation Office of Hungary (K143766, FK143233), and the Hungarian Academy of Sciences (NAP2022-I-6/2022).

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PL06
BIOMEDICAL POTENTIAL OF PHYTOECDYSTEROIDS AND THEIR SEMI-SYNTHETIC DERIVATIVES

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Ecdysteroids are the most widely distributed steroid hormones in nature and are among the most versatile groups of natural products. These compounds form a chemical bridge between arthropods, the Plant kingdom, and higher animals, with distinct and very specific functions. In arthropods, 20-hydroxy-ecdysone (20E) is well known as the moulting hormone. Plants biosynthesize a large chemical diversity of such compounds as natural pesticides. In higher animals and humans these compounds act as nonhormonal adaptogenic and anabolic agents, increase resistance to stress, and provide various health benefits. Most recently, 20E was revealed as a life-saving therapeutic agent in adults with severe COVID-19 in a Phase 2/3 clinical trial due to its ability to activate the Mas receptor.[1]

Although there are well over 500 phytoecdysteroids known until now and the possible variations suggest the existence of ca. 1000 altogether,[2] very little is known about the pharmacology of ecdysteroids other than 20E. This is mainly because the ecdysteroid composition of plants is usually dominated by this compound, and most of the chemical variability is related to minor plant components.

The above characteristics make ecdysteroids a highly valuable and largely unexplored pool for drug discovery. They may interfere with cell death and survival in either direction, i.e., using different chemical strategies, and this allows designing semisynthetic derivatives that are engineered toward potent antitumor or cytoprotective agents. For example, our recent studies demonstrated that certain ecdysteroid-containing nanoassemblies sensitize CNS-originated tumor cells to oxidative stress while protecting surrounding normal tissues.

The presentation provides an overview of our research program that expands the chemical space of ecdysteroids by combining natural product isolation, diversity-oriented, and targeted semisynthesis from industrial plant extracts marketed as herbal food supplements. Additionally, it provides new insights into the complex ecological role of ecdysteroids throughout the Kingdoms of Nature.

Acknowledgments: Financial support from the NRDIO, Hungary (K-146359) and TKP2021-EGA-32 is acknowledged.

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PL07
LOCALIZING DOUBLE AND TRIPLE BONDS IN LIPID MOLECULES BY MASS SPECTROMETRY.

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Introduction: Lipids are essential for human health, serving as vital components of cell membranes, signaling molecules, and energy sources. Their structural diversity and complexity are linked to numerous diseases. Mass spectrometry (MS) has become crucial for lipid analysis due to its high sensitivity and specificity. However, traditional MS methods often fall short of fully characterizing lipid structures. Developing new MS methods and incorporating advanced ion activation techniques are crucial for accurately elucidating lipid structures, enhancing our understanding of lipid-related diseases, and developing targeted therapeutic interventions. This work focuses on two novel MS-based approaches for localizing double and triple bonds in aliphatic chains of lipids.

Materials and Methods: Lipid standards were obtained from commercial suppliers or synthesized in-house. Lipids were ionized either by atmospheric pressure chemical ionization (APCI) in the presence of acetonitrile or by electrospray ionization (ESI) using lithium ions cationization. The ions formed in the ion sources were fragmented by collision-induced dissociation (CID) or ultraviolet photodissociation (UVPD).

Results: In the APCI source, acetonitrile formed reactive species, which added to double and triple bonds of lipids to form [M + C3H5N]+• ions. Their collisional activation in an ion trap provided structure-informative fragments. The approach was applied to fatty acids with isolated, cumulated, and conjugated double bonds and triple bonds. Several new fatty acids have been discovered in plant seeds. In the second method, lithiated lipids were formed in an ESI source. When activated by high-energy photons, these ions provided unique fragments due to photoinduced cleavages at the ester moieties and double bonds. UVPD spectra of various wax esters and triacylglycerol estolides were studied, and the method was applied to analyze wax esters from jojoba oil and vernix caseosa.

Conclusions: New analysis methods offer a more detailed characterization of the structure of bioactive lipids.

Acknowledgements: This study was supported by the project National Institute for Research of Metabolic and Cardiovascular Diseases (Programme EXCELES, ID Project No. LX22NPO5104) - Funded by the European Union - Next Generation EU.

PL08
THE ROLE OF GLUTATHIONE S-TRANSFERASE IN EPITHELIAL MESENCHYMAL TRANSITION (EMT) MODEL IN COLORECTAL CANCER AND THE ENHANCEMENT OF ADJUVANT THERAPY BY TARGETING GLUTATHIONE S-TRANSFERASE INHIBITOR

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Colorectal cancer is the third leading cause of cancer-related deaths worldwide. For colorectal cancers that have not spread to distant sites, surgery is usually the primary or first treatment option. However, chemotherapy (neoadjuvan, adjuvan and advanced-stage chemotherapy) is still widely used. Several chemotherapeutic agents are available for the treatment of CRC, but eventually cancer relapse occurs. A major impediment in the success of available therapies is the recurrent adaptation of cancer cells, leading to metastases, which are often considered as the point of no return, and are associated with the worst outcome. Therefore, understanding the mechanisms that drive resistance of cancer cells bears special importance.

Recent research suggests that resistance to chemotherapy may be significantly influenced by the transdifferentiation program known as epithelial-mesenchymal transition (EMT), which occurs naturally. It is currently unknown what possible signaling pathway links EMT to drug resistance, despite the fact that EMT has been clearly shown to be essential for chemoresistance and metastasis. Glutathione S-Transferases (GSTs), a family of isozymes that catalyze the reaction of glutathione (GSH) with electrophiles of both endogenous and xenobiotic origins, assist in the development of drug resistance through direct detoxification. The pi (π) and mu (μ) classes of GSTs play a regulatory role in cellular survival and also in development of cancer.

Therefore, an in vitro EMT model was established in the HT-29 CRC cell line for this work, and EMT was demonstrated by immunohistochemical and biochemical techniques. In the epithelial and mesenchymal phenotypic of HT-29 CRC cells, the expression and protein levels of GST-π and GST-μ were measured. In the epithelial and mesenchymal phenotypes of HT-29 CRC cells, oxidative stress was produced and oxidative damage was observed. A link between the oxidative damage and GST isoenzymes was established at the gene and protein levels. The FDA-approved GST inhibitor ethacrynic acid (ETA) was used to treat both phenotypes of HT-29 CRC cells. After ETA treatment, the GST isoenzyme expressions and protein levels were measured. To examine the impact of GST inhibitor on EMT in colorectal cancer, assays were performed again for HT-29 cells with oxidatively damaged epithelial and mesenchymal phenotypes. To test the effectiveness of the novel therapeutic approach, epithelial and mesenchymal phenotypes were treated with adjuvant therapy combination and adjuvant therapy combination with ETA. Blank and ETA loaded PLGA-*b*-PEG nanoparticles and mPLGA-PEG-SS-ETA nanoconjugates were prepared by nanoprecipitation technique. These nanoformulations were characterized in terms of mean particle size, PDI, zeta potential and morphology. ETA loading capacity and loading efficiency of nanoformulations were determined by validated HPLC method. The optimized nanoformulations were coupled with Vimentin (Vim) monoclonal antibody specific to mesenchymal phenotype of HT-29 CRC cells for targeted delivery. *In vitro* cytotoxicity of nanoformulations were determined on L929 cells. Epithelial and mesenchymal phenotypes were treated with adjuvant therapy combination plus ETA loaded and mesenchymal phenotype targeted nanoformulations to investigate the efficacy of the new targeted therapeutic protocol. *In vivo* EMT model was created in the immunosuppressed Wistar rats. Animals were treated with adjuvant therapy combination and adjuvant therapy combination plus ETA loaded and mesenchymal phenotype targeted nanoformulations to investigate the *in vivo* efficacy of the new targeted therapeutic protocol.

Using the nanoprecipitation process, blank and ETA-loaded PLGA-b-PEG nanoparticles as well as mPLGA-PEG-SS-ETA nanoconjugates were created. The morphology, zeta potential, mean particle size, and PDI of these nanoformulations were all evaluated. A validated HPLC method was used to determine the nanoformulations' loading efficiency and capacity. For targeted distribution, the improved nanoformulations were combined with a monoclonal antibody called Vimentin (Vim), which is specific to the mesenchymal phenotype of HT-29 CRC cells. Using L929 cells, the in vitro cytotoxicity of nanoformulations was assessed. To test the effectiveness of the novel targeted therapeutic approach, epithelial and mesenchymal phenotypes were treated with adjuvant therapy in combination with ETA loaded and mesenchymal phenotype targeted nanoformulations. Using immunosuppressed Wistar rats, an in vivo EMT model was developed. Vim mAb conjugation enabled the successful targeting of both nanoformulations to the mesenchymal phenotype. Even at lower doses, targeted formulations demonstrated an inhibitory effect on GST-π isoenzyme activity and exhibited higher cell uptake rates.

Immunosuppressed Wistar rats were effectively injected with HT-29 CRC cells to provide an in vivo EMT model. There was evidence of elevated GST-π isoenzyme expression in animals exhibiting EMT development. Adjuvant treatment efficacy was increased and developed granuloma diameters were decreased by ETA-loaded and mesenchymal phenotype targeted nanoformulations.

PL09
BIOFUNCTIONALIZED CARBON NANOSTRUCTURES: NEW BUILDING BLOCKS FOR THE DEVELOPMENT OF ELECTROCHEMICAL SENSORS

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Electrochemical biosensors have demonstrated to be an extremely useful analytical tool in different fields. Due to their unique properties, the incorporation of carbon nanostructures in general, and carbon nanotubes (CNTs) in particular, to the biosensing platforms, have made posible the construction of innovative and versatile electrochemical (bio)sensors for the detection of different markers.

To achieve the fully exploitation of the fascinating properties of CNTs, an exfolitation step is essential. In this regard, we propose "smart" strategies to functionalize CNTs through the rational selection of compounds that simultaneously exfoliatie the CNTs and provide with particular (bio)recognition properties transforming them in versatile building blocks for the construction of electrochemical (bio)sensors.

Typical examples will be discussed in this presentation focused on the development of sensors for the quantification of biomarkers (BRCA-1-gen, SARS-CoV-2 nucleic acid, Immunoglobulin G, oxidative stress-related compounds, glucosa) and pollutants, among others.

In summary, the rational selection of biomolecules to exfoliate the CNTs represents a very interesting alternative to build innovative and competitive biosensors without additional steps for the immobilization of the biorecognition layer. The versatility and the efficiency of the resulting architectures paves the way for further developments of simple, label-free, friendly and highly sensitive biosensors with multiple applications for biomarkers detection.

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

PL10
MEMBRANE TRANSPORTER INVOLVEMENT IN THE ABSORPTION OF INHALED DRUGS

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Virtually every cell in the body is equipped with a tightly regulated machinery of membrane transporter proteins. These transporters facilitate cellular entry or efflux of their substrates across lipid bilayers. In a biopharmaceutical context, however, the protective function of efflux transporters of the ATP-binding cassette (ABC) transporter family, e.g. P-glycoprotein (P-gp) and multidrug resistance-associated protein 1 (MRP1) sometimes negatively impacts on bioavailability, for example due to reduced gastrointestinal absorption, increased hepatic and/or renal clearance and restricted access to certain compartments, such as the CNS. Consequently, a wealth of information has been published on transporter effects in drug disposition in the intestine, liver, kidneys and the blood-brain-barrier. FDA and EMA guidelines for testing of new drug candidates reflect this knowledge base. Pulmonary membrane transporter research, however, remains a relatively understudied subject.

This presentation will discuss the interaction of several members of the ABC transporter family with inhaled drugs in pre-clinical *in vitro*, *ex vivo* and *in vivo* models.

In the lungs, the membrane transporter P-glycoprotein (P-gp) is expressed in the apical (i.e. lumen-facing) membrane of airway epithelial cells and in the luminal (blood-facing) membrane of pulmonary capillary endothelial cells. In a novel non-invasive experimental animal model based on PET imaging using wildtype and *Abcb1a/b*$^{(-/-)}$ rats, P-gp was found to decrease pulmonary absorption of the model substrates (R)-[^{11}C]verapamil and [^{11}C]-N-desmethyl-loperamide administered by intratracheal aerosolisation. Transepithelial transfer of [^{11}C]metoclopramide, on the other hand, was not or only to a small extent affected by P-gp activity, presumably due to the compound's high passive permeability. Using the same approach studying the absorption of aerosolised 6-bromo-7-^{11}C-methylpurine, a prodrug radiotracer that is intracellularly conjugated with glutathione to form the MRP1 substrate *S*-(6-(7-^{11}C-methylpurinyl))glutathione in *Abcc1*$^{(-/-)}$ rats, significant difference were observed between knockout and wildtype animals. Inhibition or absence of MRP1, which is localised to the basolateral membrane of airway epithelial cells, reduced pulmonary absorption. These results suggest that pulmonary ABC efflux transporters are important for the efficacy and safety of inhaled drugs and that their modulation may be exploited in order to improve the pharmacokinetic and pharmacodynamic performance of pulmonary delivered drugs.

PL11
DEVELOPMENT OF THE VACCINES AND NANOVACCINES AGAINST LEISHMANIASIS BASED ON THE NANOTECHNOLOGY

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Leishmaniasis is endemic in more than 102 countries, and the epidemiological situation continues to be tense. The main reasons for the widespread spread of the disease are the emergence of resistance to the drugs used as causative agents and insecticides in their vectors. Therefore, there has been increasing interest in vaccine studies among strategies for controlling leishmaniasis. There are three distinct generations of vaccines designed to combat leishmaniasis. First-generation vaccines contain killed or live attenuated parasites; second-generation vaccines contain recombinant or native antigens and live genetically modified parasites (knockout and suicidal cassettes). Third-generation vaccines are DNA vaccines. Additionally, researchers have used vector salivary proteins, dendritic cells, and non-pathogenic L. tarentolae as vaccine candidates. However, there is still no effective vaccine against leishmaniasis. Nanovaccines are a new and promising tool for promoting immunity against infectious diseases at the nanoscale. They can act as delivery vehicles that passively or actively transport various antigens into antigen-presenting cells or as helper adjuvant components that enhance immune responses when administered together with antigens. In the literature, various studies have focused on the development of nano-based vaccines against leishmaniasis.

In this direction, we investigated how different immunogenic molecules from Leishmania parasites could be used as vaccines, both by themselves and with other molecules, using the PLGA polymeric nanocarrier system. (Allahverdiyev AM et.al 2010; 2017; O.A. Tosyali et al 2021 Kelleci K, et al. 2023). In our previous study, lipophosphoglycan molecule (LPG), one of the most immunogenic antigens of Leishmania parasites, was encapsulated into PLGA nanoparticles with autoclaved (ALA) or soluble leishmanial antigens (SLA), and the effects of these compounds were investigated in vitro and in vivo. The results showed that antigen-loaded nanoparticles increased the amount of NO released from macrophages by 14- and 18-fold compared to the control, and macrophages also secreted excessive levels of the cytokines IFN-γ and IL-12. Additionally, it was determined that vaccination with antigen-loaded nanoparticles provides approximately 80% protection against Visceral Leishmaniasis. These results indicate that both (SLA-LPG)PLGA NPs and (ALA-LPG)PLGA NPs have excellent immunostimulatory activities and promise new nanovaccine formulations for the prevention of leishmaniasis in the future.

PL12
INORGANICS DOPED SCAFFOLDS FOR TENDON TISSUE ENGINEERING

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Each year, more than 32 million tendon injuries have been reported mainly caused by sports injuries, and population aging. An innovative approach for the treatment of these injuries is represented by tissue engineered bio-mimetic scaffolds able to support the host cells homing, differentiation, and proliferation. In this context, thermoplastic polymers are of special interest in the tissue engineering field as they allow the production of scaffolds with controlled elastic and mechanical properties, suitable as an effective support during the new tissue formation. However, the polymeric scaffolds alone are insufficient to guarantee a complete healing control, since they lack of adequate hierarchical structure as well as adequate mechanical, chemical, and physical properties to stand the stresses and enhance tissue regeneration. For this purpose, the use of inorganic nanomaterials as doping has gained great interest in tissue engineering applications, due to their wide range of unique properties, such as anti-inflammatory and antibacterial ones.

Given these premises, the design and the development of multifunctional platforms intended for the regeneration of the tendon tissue and doped with inorganics capable of coupling antimicrobial and proliferation enhancement properties will be described.

In particular fibrous scaffolds and highly porous 3D scaffolds have been developed. Thermoplastic polymers as polyurethane and polyhydroxybutyrate have been selected. Natural biomimetic polymers (gelatin or chondroitin sulfate) have been associated to the polymer matrix to enhance bioactive properties. Inorganic doping with cerium, copper and iron oxides gives the scaffolds superior properties of tissue reparation and antimicrobials. The multidisciplinary characterization approach including a physico-chemical characterization (SEM, fibers dimensions, TEM, surface wettability, structural characterization – FTIR, TGA/DSC, SAXS – mechanical properties, degradation properties) and a preclinical characterization (in vitro biocompatibility on tenocytes, release studies, and in vivo safety on murine burn/excisional wound model) allows to pave the way to a translation towards clinics.

Acknowledgements: The authors wish to thank the following projects NODES (NRRP MUR – M4C2 1.5 European Union NextGenerationEU GA ECS00000036); OnFoods (NRRP MUR – M4C2 1.3 European Union NextGenerationEU GA PE00000003); FORCEREPAIR, Project ID:101092243 (Horizon Europe, European Commission); Safe-n-medtech; Project ID: 814607 (Horizon 2020, European Commission).

PL13
OUT OF THE ANALYSTS´ TOOLBOX – UNCOMMON APPROACHES FOR NATURAL PRODUCTS ANALYSIS

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Natural products are of immense structural and physicochemical diversity, so that their isolation and quantitative determination won't be possible by a few selected techniques only. Most established ones are column chromatography to obtain pure compounds, or HPLC and GC to determine their concentration in diverse matrices. However, this presentation will introduce some alternative options that are not widely known, but possess unique and often advantageous properties.

In terms of isolation, Fast Centrifugal Partition Chromatography (FCPC) is such an approach. It is based on the automatized partitioning of compounds between two immiscible liquid phases. One is immobilized in the instrument by centrifugal forces, the second liquid is pumped through the system as mobile phase. As there is no solid stationary phase, no sample loss due to adsorption occurs, and the separation, even sometimes limited in efficiency, is achieved much faster. A practical FCPC application for the isolation of benzylisoquinoline alkaloids (stylopine, coptisine, etc.) from a crude *Chelidonium majus* extract will show benefits and limitations of this technique.

Supercritical Fluid Chromatography (SFC) is an emerging technique, also for natural products analysis. Supercritical CO_2 as mobile phase combines optimal viscosity and diffusion, so that UHPLC like separations are possible combined with a much "greener" character (e.g. lower consumption of organic solvents). For example, seven anthraquinones occurring in *Frangula alnus* bark could be well resolved in less than 6 min, using a sub 2-µm stationary phase and a methanol-acetonitrile mixture containing oxalic acid as modifier. Method development, validation and the analysis of real samples will be described. The same applies to an application of Capillary Electrophoresis (CE), which was successfully used for the determination of several dihydrochalcones in apple leaves. As these anti-oxidant compounds were also assayed by SFC, a direct comparison of two orthogonal techniques was possible, revealing that both fulfilled validation criteria (e.g. accuracy: CE from 95.3 – 100.6 %, SFC from 97.0 – 102.5 %) and yielded nearly identical quantitative results; yet, in terms of required analysis time (CE: 9 min) and reproducibility SFC showed to be superior.

PL14
IS THE COMBINED USE OF VOLATILE ANAESTHETICS AND RADIATION IN RADIOTHERAPY SAFE?- PRELIMINARY RESULTS ON DIFFERENT ORGANS IN VIVO.

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Introduction: Although considered safe, exposure to volatile anaesthetics (VA) has shown more and more adverse effects over the last decade. Since the joint effects of exposure to VA and ionizing radiation have not been studied before, we decided to assess DNA damage in vivo in different organs after a single exposure to the volatile anaesthetics (VAs) halothane(H)/sevoflurane-(S)/isoflurane(I) and ionizing radiation in doses used in radiotherapeutic (RT) exposure.

Materials and Methods: Considering females more damage-prone, we used 240 healthy adult Swiss albino male mice divided into 48 groups. They were exposed to either: H/S/I therapeutic doses alone (2 h); 1 or 2 Gy ɣ- radiation alone; or to combined exposure. Peripheral blood, frontal lobe brain, liver, and kidney cortex samples from five animals per group were taken immediately, 2, 6, and 24 hours after the exposure. DNA damage and cellular repair index (CRI) were analysed using an alkaline comet assay and the tail intensity (TI) parameter.

Results: Elevated TI levels for S/H were usually the highest at 6 h, and within 24 h were usually repaired for S but not H, while I treatment usually caused lower TI than in control groups. Combined exposure demonstrated usually a slightly H/S protective and I protective effect, which was stronger for 2 Gy than 1 Gy. The results suggest differences in the extent of DNA damage and repair depending on the anaesthetic used. Greater damage was found in brain cells than in kidney cells, and in combined exposure, isoflurane showed a protective effect in both types of organs and at both doses. Halothane, generally, did not show a similar protective effect.

Conclusions: Although preconditioning protection should be VA-similar, CRI and TI histograms indicated different modes of action in DNA damage creation for each VA and each organ. I/S/H preconditioning demonstrated in general protective in vivo but in some cases with damage not repaired in total during 24 hours from the single exposure. Due to the constant increase in the use of RT+VA, further studies should explore the mechanisms behind these effects, including longer and multiple exposure treatments and in vivo brain tumour models. samples should also be taken over a longer period than 24 hours to determine whether DNA repair occurs at the end of a given period of exposure or whether such a level of damage persists over a long period.

Acknowledgements: The research results were obtained using the facilities and equipment the European Regional Development Fund project KK funded (No.01.1.1.02.0007 "Research and Education Centre of Environmental Health and Radiation Protection – Reconstruction and Expansion of the Institute for Medical Research and Occupational Health").

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PL15
RECEN DEVELOPMENTS IN ENANTIOSELECTIVE ANALYSIS OF CHIRAL PSYCHOACTIVE DRUGS

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Introduction: Instrumental methods used for enantioselective analysis of chiral psychotropic compounds are based on gas chromatography (GC), high-performance liquid chromatography (HPLC), super/sub-critical fluid chromatography (SFC), capillary electrophoresis (CE) and capillary electrochromatography (CEC). These separation methods are commonly coupled with mass spectrometric (MS) detectors providing high sensitivity, universality and selectivity. Of these methods HPLC-MS(/MS) is most widely used currently. However, some other methods mentioned here may provide very effective solution for some practical problems [1].

Materials and Methods: In our studies we used HPLC-MS(/MS) in combination with polysaccharide-based chiral HPLC columns for enantioselective determination of psychoactive compounds and their phase-1 metabolites in biological materials. The compound studied include methorphan [2], 3,4-methylenedioxymethamphetamine (MDMA) [3], methylone [4], clephedrone [5] and several other new psychoactive substances (NPS).

Results: Based on the enantioselective analysis it was observed that not only dextromethorphan, but more toxic levomethorphan is also abused [2], typical C-t dependences do not adequately reflect enantioselectivity in the pharmacokinetics on the initial and lateral stages [3, 4], methylone undergoes enantioselective metabolism in the human body [4] and chloromethcatinones are chemically and stereochemically instable especially in biological matrices [5].

Conclusions: Enantioselective analysis is more demanding compared to non-enantioselective one from the viewpoint of time, efforts and resources. At the same time if correctly designed it may bring additional information and value to forensic scientists and clinical toxicologists.

Acknowledgements: This study was supported in part by Shota Rustaveli National Science Foundation of Georgia through the grant № FR-22-971 for fundamental research.

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PL16
MEDICINAL CHEMISTRY OF PURINERGIC SIGNALING: TARGETS AND DRUGS FOR CANCER IMMUNOTHERAPY

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The extracellular nucleoside adenosine is an important signaling molecule activating G protein-coupled purine P1 (adenosine) receptors. These receptors, that belong to the family of class A, rhodopsin-like GPCRs, play crucial roles in inflammation, immunity, and cancer. For example, cancer and inflamed tissues can release large amounts of the nucleotide ATP, which is immediately hydrolyzed by ectonucleotidases, upregulated on many cancer cells, leading to the production of high levels of extracellular adenosine. Subsequent activation of G protein-coupled adenosine A_{2A} and A_{2B} receptors results in cancer-promoting, angiogenic, pro-metastatic, and strongly immunosuppressive effects. Recent progress in the identification and optimization of purine receptor antagonists and ectonucleotidase inhibitors by convergent approaches, utilizing structural biology, will be presented. These tool compounds, including labeled derivatives, are used to study their targets' role in health and disease. Moreover, they have potential for further development as novel drugs.

PL17
HUMAN DIHYDROOROTATE DEHYDROGENASE (HDHODH) AS DRUG TARGET: WHO IS GOING TO WIN THE HDHODH GOLD RUSH?

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At the end of 2016, the connection between Acute Myelogenous Leukemia (AML) and *dihydroorotate dehydrogenase* (*h*DHODH), a key enzyme in *de novo* pyrimidine biosynthesis, generated considerable interest from the pharmaceutical industry as a possible new therapeutic opportunity for this *unmet clinical need*. Since the COVID-19 outbreak, the use of *h*DHODH inhibitors as *Host Targeting Antivirals* (HTA) became one of the most promising therapeutic options for COVID-19 treatment as well as other pandemic outbreaks. In 2023, the discovery of the *h*DHODH role in blocking *ferroptosis* in solid tumors cells opened other scenarios also in these fields.

In this occasion, the program active since 2010 at the University of Turin dedicated to designing innovative *h*DHODH inhibitors will be fully presented. By using an innovative bioisosteric approach supported by structure-based techniques, **MEDS433**, a potent *h*DHODH inhibitor (IC_{50} = 1.2 nM) was discovered. **MEDS433** is able to induce myeloid differentiation in AML cell lines (THP1 and U937) in the low nM range (EC_{50} = 40 and 26 nM), superior to the AML phase I/II *lead brequinar* (EC_{50} = 249 nM (THP1) and 189 nM (U937)). By leading the cell into *pyrimidine starvation*, **MEDS433** inhibits the *in vitro* replication of a large panel of viruses, with EC_{50} always in the low nM range. On SARS-CoV-2, the replication is inhibited at EC_{50} = 63 nM, being **MEDS433** five folds superior of the antiviral *Molnupiravir* (EC_{50} = 300 nM), recently approved for COVID-19.

Beside detailing the **MEDS433** design&SAR, PK, ADME, toxicity (acute/subacute on different species) as well as the *in vivo* efficacy in different AML models (leukemic xenograft and IV (mouse, IP, PO)), its synthetic technological transfer (8 g batches, purity > 98.5 %) is also presented. To reinforce the scenario, the pathway that allowed the discovery of *backups compound* **MEDS608** and **MEDS700** (EC_{50} = 31 and 17 nM (THP1) respectively), is also presented. All these studies, most of them still unpublished, are directed to open the incoming **MEDS433** certified preclinical studies necessary for preparing its Phase I clinical trial for AML.

Moving to the conclusion, the clinical scenario that involves *h*DHODH inhibitors will be detailed. In particular, the most recent strategies investigated for overcoming possible *h*DHODH resistance at the clinical level will be presented. This final step will try to answer the title question: *who will win the hDHODH golden rush?*

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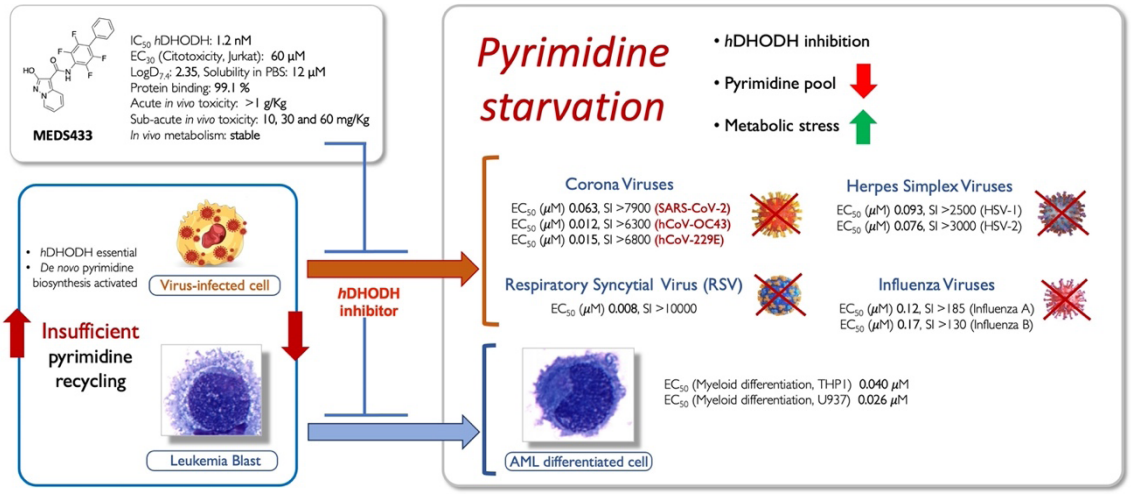

PL18
THE USE OF GOLD NANOPARTICLES AS DRUG DELIVERY SYSTEMS IN THE TREATMENT OF DRUG-RESISTANT EPILEPSY: PRECLINICAL STUDIES

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Epilepsy is one of the most prevalent chronic neurological disorders, affecting millions of individuals worldwide. The blood-brain barrier (BBB), a dynamic and highly selective barrier primarily formed by the endothelial cells of brain microvessels, strictly regulates the transport of substances between the brain and blood, thereby maintaining brain homeostasis. Epileptic seizures in humans and experimental animals are associated with BBB disruption, and the dysfunction of the BBB has been demonstrated to be both a cause and a consequence of epileptic activity. Consequently, recent therapeutic strategies have targeted the cells of the neurovascular unit. However, the majority of antiseizure drugs fail to demonstrate significant efficacy in reducing the prevalence of drug-resistant epilepsy (DRE) which affects approximately 30-40% of epileptic patients. The limited effectiveness of such pharmacologic treatments is often due to the inability of antiepileptic drugs to penetrate the brain at effective doses because of the functioning BBB which underscores the urgent need for the development of innovative therapeutic modalities to overcome the obstacle created by the BBB. In this regard, organic and metallic nanoparticle-based drug delivery systems are promising therapeutic strategies for precise BBB targeting for the treatment of DRE. In our study, we will discuss the latest developments in preclinical studies in gold nanoparticle (GNP) based delivery of antiepileptic drugs into the brain. Gold nanoparticles are also a growingly popular delivery strategy for Cas9 as a ribonucleoprotein, and GNPs-conjugated to DNA oligonucleotides have been designed as a potential tool for gene therapy.

PL19

BIODISTRIBUTION AND INTESTINAL INFLAMMATORY RESPONSE IN MICE FOLLOWING VOLUNTARY ORAL INGESTION OF SILVER NANOPARTICLES

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Introduction: The widespread use of silver nanoparticles (AgNP) in the food industry, spanning various production stages, has raised concerns about increased exposure, requiring a thorough investigation into the potential health effects, especially in the gastrointestinal tract, where high concentrations may be achieved.

Materials and Methods: This study aimed to evaluate the biodistribution patterns and potential pro-inflammatory effects of subacute oral administration of 5 nm polyvinylpyrrolidone (PVP)-coated silver nanoparticles (AgNPs) in C57BL/6J mice. AgNPs were administered at doses of 1 mg/kg body weight or 10 mg/kg body weight, once daily for 14 days, using a novel technology called HaPILLness, which allows for voluntary, stress-free, and accurate oral dosing. The evaluation included an examination of the AgNP biodistribution profile, intestinal histopathological analysis, and the quantification of a panel of cytokines and intestinal nuclear factor-κB (NF-κB) activation.

Results: Our results indicate that the intestinal accumulation of orally administered AgNP, at both doses, has the potential to trigger an inflammatory response. This response was primarily characterized by significant vascular and cellular changes, associated with the activation of the NF-κB inflammatory pathway, leading to the production of several cytokines and chemokines.

Conclusions: Our study provides new and important insights into the in vivo subacute intestinal toxicity and biodistribution of AgNP, which could significantly impact public health.

Acknowledgements: This work also received support from FCT/MCTES (LA/P/0008/2020 DOI 10.54499/LA/P/0008/2020 and UIDP/50006/2020 DOI 10.54499/UIDP/50006/2020), and from COST Action CA20121 (https://benbedphar.org/about-benbedphar/). MF acknowledges her CEEC contract-2020.04126.CEECIND/CP1596/CT0006 and LAQV-REQUIMTE for her contract under the reference LA/P/0008/2020: DOI 10.54499/LA/P/0008/2020. AS thanks FCT and ESF her PhD grant-SFRH/BD/150656/2020.

PL20
OUR CONTRIBUTION TO THE RISK ASSESSMENT OF CHEMICAL MIXTURES

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Introduction: Modern toxicology is not a "single chemical science" anymore because we are all exposed to various mixtures of both anthropogenic and naturally occurring chemicals, permanently. Starting from the time, when the toxicology studies of chemical mixtures were mainly descriptive in nature, mixture toxicology has been moving towards the application of new approach methodologies. Along with in silico toxicogenomic data mining, we aimed to study the mixture effects of toxic metals and certain persistent organic pollutants using in vivo rat model (1-4).

Materials and Methods: The Comparative Toxicogenomic Database, GeneMANIA online software, and ToppGene Suite portal were tools for toxicogenomic data mining and gene ontology analysis. Animal experiment: Wistar rats were orally exposed to the mixtures of Pb and PCBs or Cd and PCBs or Cd and BDE209 by the 3 x 3 dose design groups + control groups during the 28 days. PROAST software was used for dose-response modeling and the establishment of BMDL for toxicological endpoints.

Results: Our analysis identified genes common to all the investigated substances and linked to endocrine-disrupting outcomes. Pathway enrichment analysis identified oxidative stress response as the central disrupted molecular pathway. In vivo experiments revealed that subacute exposure to the chemical mixtures was capable of inducing thyroid and male reproductive toxicity different from the single chemical profile.

Conclusions: Our results may contribute to a better understanding of the mixture effects highly relevant for assessing the human health risk of long-life co-exposure to environmentally relevant substances.

Acknowledgements: This research was funded by the Ministry of Science, Technological Development and Innovation, Republic of Serbia through two Grant Agreements with University of Belgrade-Faculty of Pharmacy No 451-03-65/2024-03/ 200161 and No 451-03-66/2024-03/ 200161.

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PL21
CLINICAL PHARMACY EDUCATION AND PRACTICE IN EUROPE AND MALTA

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Introduction: Positive impact on patient outcomes and pharamacoeconomic implications of clinical pharmacy services have now been demonstrated (1). Clinical pharmacy relies on opportunities of clinical pharmacy education and identifying how the models of education can spearhead evolvements in practice in diverse pharmacy settings. The aims are to reflect on an overview of clinical pharmacy education evolvements in the region, describe enabling features and resources that contribute towards delivering clinical pharmacy education and practice developments, and highlight pharmaceutical workforce capacity building in clinical pharmacy.

Materials and Methods: The introduction of clinical pharmacy services in Malta was a direct influence from the movement in the USA and started in the early 1970s. This was achieved through a collaborative model where academia supported practice sites and provided opportunities for evolving knowledge, skills, attitude and competences applicable to transforming pharmaceutical services provided in hospital and community pharmacies. The initiative led to the development of a patient-centred curriculum leading to a degree in pharmacy where students participate in experiential learning in clinical sites including hospital pharmacy, community pharmacy and ambulatory care from the early years in the educational programme. The transformative pharmacy education was a facilitator for the establishment of post-graduate clinical pharmacy education.

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Results: Enabling features and resources include faculty development through inter-professional collaboration and networking amongst higher education institutions and practice sites, integration of pharmaceutical sciences with clinical pharmacy education and elaboration of pharmacy practice research (2). Post-graduate clinical pharmacy education that supports the development of people-focus practice within the context of leadership and innovation, is a means to increase the pharmaceutical clinical pharmacy workforce and support transformation of services and the profession. Examples where clinical pharmacy services have been established in practice following the educational transformation are identified in supporting pharmacist contribution in self-care medication, in optimizing chronic medication, in meeting pharmaceutical needs of special populations such as older persons.

Conclusions: Opportunities of clinical pharmacy education focus on ensuring that pharmacists develop the competences that are necessary to contribute to optimization of pharmacotherapy and ensuring patient safety. The goal of empowering pharmacists on a global scale to access clinical pharmacy education and contribute to innovative pharmacy practice models is a contribution towards the healthcare landscape.

PL22
ATTAINING COMPETENCY TO DELIVER PATIENT-FOCUSED CLINICAL SERVICES

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Introduction: Pharmacy practice in the United States has undergone major transformation since the 1960's. Pharmacists around the world are now embracing new roles focusing on patient pharmacotherapy in different patient care settings. The responsibilities of pharmacists have been extended from products and dispensing towards rational pharmacotherapy aimed to attain the most optimal outcomes. Comprehensive medication management is often conducted by clinical pharmacists as they practice in interdisciplinary teams in collaboration with physicians and other health care professionals. The requisite competencies needed to deliver these evolving responsibilities effectively include: direct patient care, pharmacotherapy knowledge, system-based care and population health, communication, professionalism and continuing professional development. There are different pathways and education opportunities available to nurture the development of these and other competencies. Certification examination is often used to indicate attainment of competency needed for specific clinical practice specialty. In several countries, board certification is being used by health authority and/or institutions as a benchmark for clinical pharmacist appointment and/or career advancement. Such framework for pharmacists' practice specialization and development has facilitated the expansion of clinical services, advancement of clinical pharmacy practice, personal professional development and significantly, the recognition of contributions by clinical pharmacists within the health care enterprise.

PL23
MIGHT PLANTS FROM WESTERN AFRICA AND SOUTHEAST ASIA BE THE HIDDENGEMS FOR ANTI-INFLAMMATORY THERAPIES? AN 8-YEAR RESEARCH JOURNEY FROM TRADITIONAL USE VALIDATION TO DISCOVERY OF NEW PRECLINICAL CANDIDATES

Gomes, NGM.

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Introduction: Scientific expeditions carried out in Guinea-Bissau and Thailand enabled the collection of plant material of over 110 species from Southeast Asia and Western Africa, many of which previously unknown to science on their chemical composition and pharmacological effects. Driven by an ethnopharmacological approach, the aim was to validate ethnomedicinal uses, valorize species for herbal drug development, and identify preclinical candidates for anti-inflammatory therapy.

Materials and Methods: Chemical characterization was performed using conventional hyphenated chromatographic techniques (e.g., HPLC-DAD-ESI/MSn), while indicative pharmacological assays (enzymatic and cell-based) targeting pro-inflammatory mediators and oxidative stress were selected to provide preclinical data on anti-inflammatory efficacy.

Results: Selected scientific outcomes include the corroboration of the traditional use of Homalium bhamoense bark in skin wound healing (Suksungworn et al., 2020) and the previously empirically attributed antidiabetic effects of Caryota urens, which proved to be more efficient than the blockbuster drug acarbose (Andrade et al., 2023). It was also found that the anti-inflammatory effects of Cassia sieberiana mainly rely on quercetin, interfering with a series of pro-inflammatory mediators in THP-1 cells, namely interleukin-6 (Macedo et al., 2021). Additionally, naringenin-8-sulphonate, obtained from Parinari excelsa bark, was discovered and established as a novel anti-inflammatory lead candidate (Macedo et al., 2023).

Conclusions: This 8-year journey based on an ethnopharmacological approach enabled the validation of the traditional use of over 25 plant species from Western Africa and Southeast Asia. This scientific rationale also translated on the valorization of herbal supplements that are currently commercially available, as well as the discovery of a new advanced preclinical candidate for anti-inflammatory therapy. Cumulatively, the research line driven by an ethnopharmacological approach, established in 2016 at LAQV/REQUIMTE, continues to corroborate the utility of traditional medicinal knowledge on drug discovery, particularly in enriching the clinical pipeline with drugs to aid in conditions with an inflammatory background.

Acknowledgements: This work received financial support from FCT/MCTES (UIDB/50006/2020 DOI: 10.54499/UIDB/50006/2020) through national funds. Nelson G. M. Gomes thanks FCT (Fundação para a Ciência e Tecnologia) for funding through the Scientific Employment Stimulus Individual Call (Ref. 2022.07375.CEECIND); https://doi.org/10.54499/2022.07375.CEECIND/CP1724/CT0013. The presented scientific outcomes build on the collaborative efforts of numerous researchers.

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PL24
TRACE ELEMENTS – DO THEY HAVE A ROLE IN THE CLAIMED THERAPEUTIC EFFECT OF MEDICINAL PLANTS?

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It is estimated that between 35,000 to 70,000 plant species are or have been used for medicinal purposes around the world (1). This widespread use of medicinal plants even motivated the publication by the WHO of a long series of monographs on selected medicinal plants, where their medicinal uses (whether "uses supported by clinical data", "uses described in pharmacopoeias and systems of traditional medicine" or "uses described in folk medicine, not supported by experimental or clinical data") are compiled (2). These monographs also report the major chemical constituents and the pharmacological bases of the therapeutic effects of these plants. Invariably these are justified by the presence of a wide range of pharmacologically active organic compounds.

However, several chemical elements, including several trace elements, are essential nutrients, with notable beneficial effects on the human body at different levels, from metabolism in general, to the immune system or antioxidant/antidegenerative defense (3). And it is known that different plant species can uptake and accumulate different amounts of trace elements (4). Therefore, it is reasonable to think that the claimed therapeutic effects of medicinal plants could be, at least in part, due to a particularly high content of essential trace elements (which would make them a rich source of these nutrients) (5).

This communication will review the most recent scientific evidence on the beneficial health effects of macrominerals and essential trace elements and the recent literature on the content of trace elements in medicinal plants. Particular cases where a possible role of trace elements in the claimed therapeutic effects of medicinal plants may be present will be highlighted.

Funding: This work received financial support from FCT/MCTES (UIDB/50006/2020 DOI 10.54499 / UIDB/50006/2020) through national funds.

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PL25
NUCLEAR RECEPTORS AS TARGETS FOR NATURAL PRODUCT (ANALOGS)

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Nuclear receptors (NR) are ligand-responsive transcription factors. They share a conserved structure with a ligand binding domain, a DNA binding domain and transactivation functions. Due to their regulations by ligands these receptors are interesting drug targets [1, 2]. In humans 48 NR are known. Endogenous ligands mainly originate from the fatty acid and isoprenoid metabolism proposing natural products as likely candidates for ligands. The retinoic acid receptor-related orphan receptors (ROR) belong to the Type IV NRs acting as monomers. They are constitutively active allowing the search for inverse agonists. They also are not officially de-orphanized, although cholesterol biosynthetic intermediates and oxy-cholesterol derivatives can bind and act as ligands. One subtype, RORγt, plays a crucial role in Th17 differentiation and its cytokine production (IL-17, IL-22) and is therefore an attractive target for inverse agonists in inflammatory disease and for agonists in immuno-oncology. Our group works on the identification of natural product-based ligands for ROR receptors. Two examples will we presented in the talk.

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PL26
AURAPTENE: FROM ITS DISCOVERY TO CLINICAL TRIALS

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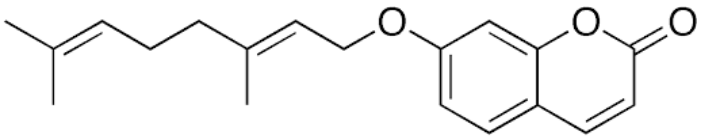
Auraptene (7-geranyloxycoumarin) 1 is the most representative compound of a rare class of natural products, the oxyprenylated phenylpropanoids.



1

Even though it has been isolated for the first time in 1930 from the peels and skin of fruits of *Citrus aurantium* L. (bitter orange), only in the last two decades this secondary metabolite has been subject of intensive research aimed at better characterizing new natural sources, its phytochemical and nutraceutical properties, and to get more insights into its biological activity and therapeutic potential. Like in a fairy tale with a happy ending lasting more than 20 years, auraptene has been characterized among the most interesting and promising active principle that can be obtained from a wide panel of plant sources.

At the very beginning of this "tale", a single easy to handle and high yielding synthetic step made auraptene **1** available in gram scale so that several *in vitro* pharmacological assays could be performed. Thus, it has been found how compound **1** exerted numerous beneficial effects mainly as an anti-inflammatory, anti-cancer, and neuroprotective agent. Moving to *in vivo* tests using suitable and predictive animal models such properties have been confirmed. In parallel, apart from the "classic" plant sources belonging to the Rutaceae family, investigations revealed how auraptene represented an additional component of the phytochemical pool of medicinal, healthy, and food plant species known to have beneficial properties for human health and for the dietary feeding prevention of acute and chronic syndromes. The overall data accumulated over the last 20 years did encourage the performance of a clinical trial in humans using phytopreparations derived from fruits of *Citrus limon* standardized in their composition for auraptene and total flavonoids as a nutraceutical remedy for the prevention of Alzheimer's disease.

PL27
EVIDENCE BASED ANTI-AGING PHYTOTHERAPY

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Evidence based phytotherapy (EBP) can be defined as "the use of the scientific method to organize and apply current phytotherapy data to improve health-care decisions". The elements of EBP process can be summarized in 6A (ask, acquire, appraise, analyze, apply, assess/audit) cycle after determination of the problem. The question (ask) can be formulated in PICOTS (Patient/Population/Disease, Intervention, Comparison/Comparator, Outcome, Time frame, Setting) format and searched in Tripdatabase, Cochrane Library, Pubmed etc. After acquiring, data can be appraised/used to create an evidence base. Evidences are analyzed/rated. Some already scored evidences can be found in databases like MedlinePlus (a service of the National Library of Medicine), Natural Medicines Comprehensive Database, and National Center for Complementary and Integrative Health. Natural Medicines Comprehensive Database rates effectiveness and safety for any indication. Any natural product that meets "effective or likely effective" and "likely safe" criteria for any indication can be recommended. The hierarchy of evidences are represented by 5S evidence pyramid (from down to top: studies, syntheses, synopses, summaries, systems). The best relevant evidences are applied and results are assessed. Phytotherapy can be used to slow down, stop, or reverse aging or age related diseases. Any anti-aging phytotherapeutic is expected target any of "twelve hallmarks of aging: genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, disabled macroautophagy, deregulated nutrient-sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, altered intercellular communication, chronic inflammation, and dysbiosis". Since aging is complex, model organisms like *Caenorhabditis elegans* (*C. elegans*) are commonly used to add evidences by testing natural products' anti-aging effects. As an example, we found that aloe-emodin can extend lifespan of *C. elegans*. Phytoherapeutics, especially the ones reported as panacea or tonic, from traditional/ancient medicine and secondary metabolites from long living plants/seeds can be promising candidates for new evidence based anti-aging interventions.

PL28
A NEW MECHANISM FOR ESTROGEN-INDUCED FACILITATION OF ARRHYTHMIAS IN THE LONG QT SYNDROME

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Background: Estrogens have been reported to depress IKr and ICaL, two actions with potentially opposite effects on repolarization and arrhythmogenesis in genetic long-QT syndromes (LQTS). In a female LQT2 patient (HERG mutation), therapeutic administration of β2-estradiol (E2) was associated with ventricular arrhythmias and syncope. Aim: to investigate the mechanism of E2 arrhythmogenic effect in the context of LQT2. Methods: We obtained hiPS-derived cardiomyocytes (hiPS-CMs) from the LQT2 patient and studied them by whole-cell patch-clamp. Experimental findings were incorporated in a computational model.

Results: The HERG mutation phenotype was fully expressed in LQT2 hiPS-CMs. In these myocytes, but not in wild type ones, exposure to E2 shortened action potential duration (APD) but paradoxically facilitated early afterdepolarizations (EADs). We detected ICaL gating abnormalities in LQT2 hiPS-CMs, which were further modulated by E2 in a way suitable to account for APD shortening and EADs facilitation at the same time. E2 had no effect in WT hiPS-CMs. The E2 effect was reproduced by inclusion of the ICaL gating abnormalities in a LQT2 computational model.

Conclusions: the HERG channel mutation was associated with ICaL gating changes partially countering mutation's effect on APD, but further destabilizing repolarization. This implies a crosstalk between mutant K+ channels and Ca2+ ones, both unexpected and of proarrhythmic significance, whose mechanism deserves further investigation.

PL29
HETERORESISTANCE

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The antimicrobial susceptibility tests we use in microbiology laboratories classify isolates as susceptible or resistant, assuming that a bacterial isolate is a uniform entity. However, an isolate may consist of subpopulations with different phenotypic characteristics, such as different antimicrobial susceptibility patterns, which is a challenge for microbiology laboratories and clinicians.

Heterogeneous antibiotic resistance was first described in *Haemophilus influenzae* in 1947. However, the first reported use of the term "heteroresistance" was in 1970. Heteroresistance is a phenotype in which a susceptible population of bacteria contains a small subpopulation of cells that are more resistant than the main population.

Antimicrobial susceptibility methods (MIC determination, disc diffusion...) and standard criteria for defining isolates as susceptible, resistant or intermediate resistant to each antibiotics are generally agreed worldwide. On the other hand heteroresistance is poorly characterized and there is a lack of standards for the definition of it. The methods used to determine heteroresistance vary widely between laboratories. Heteroresistance has been described for many antibiotics (methicillin, vancomycin, carbapenem, colistin, tetracyclines, aminoglycosides, quinolones and etc) & for many species of bacteria (*Staphylococcus aureus, Klebsiella pneumoniae, Escherichia coli, Acinetobacter baumannii, Pseudomonas aeruginosa, Enterobacter cloacae and etc).*

Although heteroresistance has been observed worldwide in a wide variety of pathogens and in response to numerous classes of antibiotics, there is very little epidemiological data about its prevalence. The prevalence of heteroresistance varies depending on the study and the methodology used.

As the frequency of the resistant subpopulation is too low to be to be detected with a standard inoculum, theantimicrobial susceptibility methods cannot accurately distinguish heteroresistant bacteria. Population analysis profile (PAP) assay is the gold standard method for detection of heteroresistance. However, it is time-consuming and labour-intensive and there is a lack of standardised assessment criteria, which makes the method unsuitable for clinical use.

Its clinical impact still remains unclear for most bacterial species. There is a need for further studies to establish the relationship between heteroresistance and clinical outcomes.

PL30
TREATMENT OF DIABETIC NEPHROPATHY WITH SGLT2 INHIBITORS – DOES SEX MATTER?

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Introduction: Chronic kidney disease (CKD) is a progressive condition leading end-stage renal failure, a necessity of dialysis treatment, and ultimately premature death. Diabetes is a leading cause of CKD. Sodium-glucose transporter 2 (SGLT2) inhibitors are antidiabetic drugs that mitigate the development of CKD in both diabetic and non-diabetic patients (1).

Materials and Methods: We have systematically reviewed studies of SGLT2 inhibitors as treatments in rodent models of diabetic nephropathy (2). Based on the outcome of this review, a research program in female rats was initiated.

Results: 105 eligible studies were identified that included mouse and rat models of type 1 and type 2 diabetes, various SGLT2 inhibitors, immediate, early and late start of treatment relative to onset of diabetes. SGLT2 inhibitors consistently improved glucose homeostasis and renal function as well as multiple mechanistic parameters. However, only 4 studies were performed in female animals, and half of them did not report beneficial outcomes. Therefore, a program was initiated specifically studying parameters consistently reported to be improved in male rodents in female rats. While this program is ongoing, initial results will be presented.

Conclusions: Our initial results support only partly support improvement of renal function in female diabetic rats. This is corroborated by a recent direct comparative study of canagliflozin in both sexes, where the drug had beneficial effects in male but not female mice (3).

Acknowledgements: The underlying animal studies were supported by a grant of TUBITAK (SBAG-115S564). Renal assessments were supported by a grant of the Deutsche Forschungsgemeinschaft (We 5779/2-3). AA is supported by a fellowship of the Deutscher Akademischer Austauschdienst.

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PL31
UNRAVELING PHARMACEUTICALLY RELEVANT OLIGOSACCHARIDES: INSIGHTS FROM NMR CHARACTERIZATION

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The growing interest in diverse carbohydrates stems from their multitude of beneficial health properties, biocompatibility and widespread availability. However, within the realm of natural products, carbohydrates present notable challenges in characterization due to their complex structures. Consequently, the food and pharmaceutical industries require rapid and reliable yet non-destructive analytical techniques for effectively assessing their structures.

NMR spectroscopy stands out as an effective method for rapid and non-destructive analysis, offering detailed and direct structural insights into samples, enabling the simultaneous detection and quantification of byproducts, impurities, and residual reagents. Moreover, NMR spectroscopy, despite being categorized as a relatively insensitive technique, furnishes intricate structural details, especially beneficial in detecting subtle differences among isomeric carbohydrates. Its ability to provide the most comprehensive structural information underscores its significance in analytical chemistry.

This presentation will showcase ongoing projects in our lab, focusing on using NMR for characterizing bioactive oligosaccharides. We will discuss the challenges in characterizing microheterogeneous glycosaminoglycans and their detailed structural analysis during degradation. Additionally, we present a straightforward and non-destructive NMR technique for determining the substitution pattern of 2-hydroxypropyl-β-cyclodextrin and sulfobutylether-β-cyclodextrin, the two key pharmaceutical excipient oligosaccharides. Lastly, we aim to highlight the utility of NMR in characterizing human milk oligosaccharides, emphasizing its extensive use in distinguishing isomeric structures through techniques like ^{1}H-^{15}N HSQC NMR.

Acknowledgements: This project has received funding from the European Union's Horizon Europe research and innovation programme under the Marie Sklodowska-Curie grant agreement Bicyclos N° 101130235.

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PL32
BIOLOGICALLY ACTIVE COMPOUNDS OF ASTRAGALUS GENUS PLANTS OF UZBEKISTAN

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One of the fundamental and prioritized areas in the pharmacological development of the Republic of Uzbekistan is the production of medicines - for the pharmaceutical industry - from plant materials of local flora.

The aim of this research is to investigate the triterpenoids of *Astragalus* with the goal of developing a medicinal product for the pharmaceutical industry in Uzbekistan.

The phytochemical potential of plants in Central Asia is rich and diverse. Plants containing cycloartane triterpenoids and glycosides have been widely used in traditional medicine for various diseases. Many *Astragalus* genus plants have hypolipedemic, hypotensive, diuretic, anti-inflammatory, sedative, analgesic, immunostimulating, and cardiotonic activities. *Astragalus* (Fabaceae family) are widespread in the Republic of Uzbekistan - they number about 250 species and are a source of cycloartane triterpenoids [1, 2].

We are systematically studying *Astragalus* plants to analyze the content of plant isoprenoids, with cycloartane glycosides being predominant among them.

Out of over 25 *Astragalus* species examined, we have identified more than 170 natural compounds. Among these, 80 compounds were new and discovered first by our research team.

Materials and Methods: The chemical structures of substances was determined using spectral analysis methods including ^{1}H NMR, ^{13}C NMR, 2D and IR spectroscopy, column and HPLC chromatography.

Results: We have developed methods for the chemical transformation of cycloartane glycosides, leading to the production of several modified active compounds. Pharmacological studies conducted on both natural cycloartane glycosides and their synthetic analogues have revealed numerous compounds exhibiting a broad spectrum of biological activity.

The presentation demonstrated the biological activity of glycosides from various *Astragalus* species, including cycloorbicosides A and C obtained from *A.orbiculatus*, cyclosiversioside A, isolated from *A.sieversianus*, astragaloside VII - from *A.kuhitangi*, and cyclosiversioside F isolated from *A.pterocephalus* [3, 4].

In the research conducted by pharmaceutical scientist at the Institute of Chemistry of Plant Substances, it was established that cycloartane glucosides demonstrate cardiotonic activity and offer several advantages over cardenolides due to their lack of toxicity and absence of cumulative effects.

Cyclosieversioside F (astragaloside IV) has been shown to exhibit antioxidant, immunostimulating and hepatoprotective effects on the blood clotting system [3, 4].

In tests using animals with experimental endogenous hypercholesterolemia, askendoside C and D demonstrate high hypercholesterolemic activity.

Conclusion: The research is aimed at developing and obtaining new and effective medicinal compounds isolated from plants of Uzbekistan, since the use of natural medicines and dietary supplements is increasing in the world.

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PL33
THE IMPACT OF CELL FUSION ON GENOMIC INSTABILITY IN CANCER

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The biological phenomenon of cell fusion is mandatory for several physiological processes, such as fertilization, placentation, myogenesis, osteoclastogenesis and wound healing/ tissue regeneration. Besides, fusion processes are also mandatory for infection of host cells with enveloped viruses and have further been associated with cancer initiation and progression. Even though the fusion of two (and more) cells appears simple, like merging soap bubbles, the entire process is highly complex, tightly and timely regulated, and still not fully understood. Fusion of somatic cells is more complex than fusion of gametes due to the presence of an additional centromere. If bi- and multinucleated cells divide, this process is associated with chromosome segregation errors, lagging chromosomes, DNA damage, multipolar divisions and multinucleation, which is attributed to the additional centromere copy and additional spindle poles. All these processes run in a unique and unpredictable manner, which ultimately results in an increased genomic instability of hybrid cells. In the present study, the number of aberrant mitotic processes was quantified in early and late passage M13 hybrid cells that were derived from spontaneous homotypic fusion events of the non-malignant M13SV1 human breast epithelial cells. Briefly, the number of bi- and multinucleated cells was markedly higher in M13 hybrids. Similarly, M13 hybrids exhibited an increased degree of DNA and DNA damage, which was further associated with a higher level of deformed nuclei. Interestingly, M13 hybrids have undergone epithelial-to-mesenchymal transition and formed significantly more colonies and mammospheres than normal non-malignant M13SV1 human breast epithelial cells. Briefly, the number of bi- and multinucleated cells was markedly higher in M13 hybrids. In summary, the merger of non-malignant cells can give rise to prospective malignantly transformed hybrid cells, which is most likely attributed to cell fusion related genomic instability.

PL34
MITOCHONDRIA TRANSFER FROM MESENCHYMAL STEM CELLS CONFERS CHEMORESISTANCE TO GLIOBLASTOMA STEM CELLS THROUGH METABOLIC REWIRING

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The poor prognosis of glioblastomas (GB) is linked to their high heterogeneity and metabolic plasticity and to the presence of glioblastoma stem cells (GSCs), which support resistance to therapy, notably to temozolomide (TMZ). The recruitment of mesenchymal stem cells (MSCs) to GB also contributes to GSC chemoresistance, by mechanisms still poorly understood.

We have shown that MSCs transfer mitochondria to GSCs through tunneling nanotubes and that mitochondria transfer enhances GSCs resistance to TMZ. Metabolomics and isotopic profiling analyses revealed that mitochondria transfer induces a metabolic reprograming in GSCs, with a rewiring of the TCA cycle from glutaminolysis to reductive carboxylation as well as with an increase in orotate turnover and in pyrimidine and purine synthesis. Metabolomics analysis of GB resected tissues also documented increased concentrations of AMP, CMP, GMP and UMP nucleotides at relapse after TMZ treatment, corroborating *in vitro* analyses. By inhibiting the orotate producing enzyme dihydroorotate dehydrogenase (DHODH) with Brequinar (BRQ), we could restore TMZ sensitivity to GSCs with acquired mitochondria. We thus identified a mechanism for GB resistance to TMZ induced by mitochondria exchange with the tumor microenvironment and revealed a metabolic dependency of chemoresistant GSCs, which opens therapeutic perspectives based on synthetic lethality between TMZ and BRQ.

PL35
DRUG DESIGN AND DISCOVERY AGAINST ADVANCED CANCERS OF UNMET MEDICAL NEED – THE ROLE OF MEDICINAL CHEMISTRY

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Introduction: Medicinal chemists play crucial roles in preclinical cancer drug design and discovery. They work in close collaboration with experts in cancer biology to optimize targeted drug candidates in the hit-to-lead stage of drug discovery through structure-activity relationship (SAR) studies, towards the identification of a potential clinical candidate. Alongside their expertise in compound analogue synthesis and characterization, medicinal chemists are expected to understand and contribute towards areas such as drug target validation, target binding studies, and understanding in vitro/in vivo efficacy assays to identify lead molecule(s) as part of the drug discovery team within areas of unmet medical need [1]. In this presentation, the role of the medicinal chemist will be illustrated through the development of a novel lead BCL3 inhibitory small molecule as a case study from our own laboratories [2]. The BCL3 protein was originally identified in solid tumours as a regulator of the NF-kB transcription factor pathway, and a potential drug target driving metastasis in poor prognosis breast cancer models [3]. More recent studies have identified the role of BCL3 in driving additional signaling pathways including WNT/b-catenin; and studies have expanded interest in BCL3 as a drug target in other advanced malignancies such as colorectal cancer [4,5].

Results and discussion: We built and computationally modelled the interface between BCL3 and its cognate binding partner p50, identifying a novel binding pocket for virtual screening. Following extensive docking, scoring and preliminary laboratory testing of virtual hit molecules, we identified an anthranilic acid derivative (JS6) as a hit compound meeting our initial product profile criteria, including anti-metastatic activity in an *in vivo* model of breast cancer. Further hit-to-lead optimization led to clinical candidate TNAT-101, an orally bioavailable BCL3 inhibitor with an outstanding pre-clinical efficacy profile in a range of breast and colorectal cancer models. TNAT-101 additionally possesses a wide therapeutic window, and PK properties compatible with daily oral dosing as a first-in-class agent for clinical development, backed by a robust IP protection portfolio.

Acknowledgements: We gratefully acknowledge the support of TNA Therapeutics Inc., as license holders for the Bcl3 inhibitor IP and project portfolio.

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PL36
SELECTIVE CARBONIC ANHYDRASE INHIBITORS AS NEW ANTIBACTERIAL AGENTS WITH ANTI-HELICOBACTER PYLORI ACTIVITY

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Introduction: With the advent of the antibiotic era, the overuse and inappropriate consumption and application of antibiotics have driven the rapid emergence of multidrug-resistant pathogens. It is therefore important to develop new anti-bacterial drugs with novel mechanisms of action. The carbonic anhydrase (CA) family represents an attractive novel family of targets for treatment of infectious diseases. Until recently, only α- and β-CAs were considered to be present in Helicobacter pylori. They work in a complex interplay with urease (1). Thus, CA inhbition can be an innovative approach to tackle antibiotic resistance.

Materials and Methods: The synthesis of several inhibitors was accomplished via classical and microwave-assisted procedures keeping into consideration the presence of specific Zinc Binding Groups as the main feature. We then used four strains of *H. pylori*, the commercial strain NCTC 11637 and three clinical isolates (F1, 23, F40/499), which were characterized using metronidazole, clarithromycin, and amoxicillin as benchmarks. In vivo experiments were performed with *G. mellonella* larvae.

Results: Different chemical scaffolds (phenols, sulfonamides and derivatives, coumarins) were designed and investigated in order to assess inhibitory potency and isoform selectivity. Further microbiological (MIC/MBC, anti-biofilm effect, checkerboard test) and toxicological (LD_{50}) investigations in vitro, in silico and in vivo were performed on the best-in-class derivatives.

Conclusions: Interestingly, there are convincing literature data, which prove that interference with the CA activity from various bacteria leads to an impairment of the bacterial growth and virulence, which in turn gives a significant anti-infective effect.

Acknowledgements: This study was supported by a grant from the Italian Ministry of University and Research for financial support under the FISR program (FISR_04819 BacCAD).

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PL37
CLINICAL PHARMACY SPECIALTY TRAINING IN TURKEY

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Introduction: Clinical Pharmacy is a health specialty that defines the work of ensuring, developing and disseminating the rational and appropriate use of medicines and medical devices. Clinical pharmacy provides patient-oriented pharmacy services aiming the rational use of drugs in every field where the profession is practiced. Globally, it has been developing since the early 1960s.

Materials and Methods: Studies in the literature show that clinical pharmacists have been making significant contributions to patient health and health economics for many years with many practices.

Results: In Turkey, with the amendment made to the Law on Pharmacists and Pharmacies (dated 1953 and numbered 6197) on 14 November 2014, Turkish Ministry of Health's Board of Pharmacy Specialties was established and Clinical Pharmacy was considered as a specialty area in the field of pharmacy. Board of Pharmacy Specialties released the 'Regulation on Specialty Education in Pharmacy' on 21.10.2016. The first 'Pharmacy Specialty Entrance Exam' was held in September 2017 by the 'National Center for Student Selection and Placement' and the first clinical pharmacy specialty students started their training in 2018.

'Clinical Pharmacy Specialty Training Programs' are authorized by the Ministry of Health's Board of Pharmacy Specialties and organized by the pharmacy faculties. Currently, there are 10 authorized Clinical Pharmacy Specialty Training Programs in Turkey. Clinical Pharmacy Specialty Training Program is a three-year program consisting of theoretical and practical education, and thesis-work. At the beginning of the specialty training, one-month compulsory theoretical basic clinical pharmacy training is given by trainers from the Faculty of Pharmacy. Compulsory 'clinical environment trainings' which last for 22 months, take place in the healthcare delivery environment at affiliated hospitals; and are carried out under the supervision of authorized trainers. There is also a one-week theoretical training before each clinical environment training round regarding the relevant clinical environment. After completion of the compulsory 'clinical environment training', student focuses on thesis work and during this period (7 months), s/he can repeat one or more clinical environment trainings to reinforce her/his knowledge and skills.

Conclusions: In order to train competent clinical pharmacists, a system selecting and placing the most suitable students, providing them with quality training is established and continuously being improved. Inclusion of clinical pharmacy specialty in routine patient care in all practice areas would improve patients' health outcomes.

PL38
DEVELOPMENT, IMPLEMENTATION AND EVALUATION OF OBJECTIVE STRUCTURED CLINICAL EXAMINATIONS (OSCES) WITHIN THE IQPHARM PROJECT AT UNIVERSITY OF SARAJEVO – FACULTY OF PHARMACY

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Introduction: Lately, pharmacy education in Bosnia and Herzegovina has undergone significant changes to keep pace with healthcare innovations and become a more patient-oriented profession. Within the Erasmus + CBHE project entitled "Innovating quality assessment tools for pharmacy studies in Bosnia and Herzegovina (IQPharm project)" objective structured clinical examinations (OSCEs) are being developed as standard tests at the end of undergraduate pharmacy studies at public universities in Bosnia and Herzegovina. We aimed to describe the development, implementation, and evaluation of the OSCE model in the undergraduate pharmacy degree at the University of Sarajevo - Faculty of Pharmacy.

Materials and Methods: The OSCE's activities were conducted through the following stages: teaching staff training, developing the OSCE blueprint, OSCE pilot implementation, OSCE implementation and evaluation.

Results: The OSCE implementation was carried out at the University of Sarajevo - Faculty of Pharmacy from May 29 to June 1, 2023. The implementation of OSCE was attended by 37 teaching staff members from the University of Sarajevo - Faculty of Pharmacy. A total number of 91 fifth-year students took the OSCE exam. Before the OSCE implementation itself, teaching staff underwent training workshops and afterward, were assigned to 7 teams to prepare questions that were in individual stations (7 workstations) in accordance with the OSCE blueprint (5 interactive and 2 non-interactive stations). The OSCE Blueprint is based on the Blueprint of the University of Split School of Medicine (Croatia) and the new Competency Framework for Pharmacists by the Pharmacists Chamber of the Federation of Bosnia and Herzegovina. Also, before the OSCE implementation, a pilot OSCE was conducted on 21 fourth and fifth-year students which aimed to identify potential problems in the organization and to help them remove those before conducting on a large number of students. After the OSCE exam, the results were evaluated, and the process of implementing the OSCE itself was discussed. All students rated the test as a very stressful experience, but they are grateful for the opportunity to test their clinical and practical knowledge. The teaching staff will use the results to improve the current curriculum of subjects and ensure high standards and quality of pharmacy studies.

Conclusions: The successful implementation of the OSCEs represents a big step forward for the University of Sarajevo – Faculty of Pharmacy as well as a new era for pharmaceutical education in Bosnia and Herzegovina.

Acknowledgements: The activities described were carried out within the project "Innovating quality assessment tools for pharmacy studies in Bosnia and Herzegovina / IQPharm" co-funded by the Erasmus + Programme of the European Union (Project Reference: 618089-EPP-1-2020-1-BA-EPPKA2-CBHE-JP).

PL39
COUPLING ELECTROCHEMISTRY AND MASS SPECTROMETRY – A VERSATILE METHOD FOR THE INVESTIGATION OF METABOLIC PATHWAYS OF DRUG SUBSTANCES

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The elucidation of the metabolic fate of drug candidates is one of the major challenges in pharmaceutical research. The main route of drug elimination is an enzymatic biotransformation. These are frequently initiated by oxidation reactions ("phase I metabolism"), which are catalyzed by enzymes of the cytochrome P450 superfamily. With a strongly increasing number of novel chemical entities in recent years, rapid screening techniques that provide both reliable and easily accessible information about the biotransformation of a drug candidate are required. This is particularly valid for reactive metabolites, which are important to assess possible liver toxicity of new drug candidates. Therefore, the development of new methods for rapid screening of drug candidates in early phases is required.

Electrochemistry (EC) is one of the classical methods to induce oxidation reactions. Typical cells for electrochemistry coupled to mass spectrometry are amperometric and coulometric cells, both of which are associated with different advantages and disadvantages.

It seems obvious to employ EC as simulation technique in drug metabolism studies. Electrochemical flow-through cells coupled on-line to analysis techniques such as electrospray mass spectrometry with or without previous liquid chromatographic separation have nowadays become the technique of choice for these simulation experiments, since they may provide exhaustive information about the nature of the electrochemically generated metabolites.

The detection of reactive metabolites using conventional in vivo and in vitro techniques is hampered because the intermediately formed reactive species are prone to covalent binding to cellular macromolecules. In contrast, the on-line coupling of an electrochemical reactor with liquid chromatography/mass spectrometry (EC/LC/MS) allows the direct detection of reactive metabolites of pharmaceuticals, which are all known for readily binding to cellular macromolecules after metabolization by cytochrome P450 enzymes.

The respective experimental approaches, applications and possible future trends are presented in this work. Particular focus is directed to the electrochemical cells with different dimensions and working electrode materials and to further coupling reactions of the obtained reactive metabolites with trapping agents as glutathione or with biomacromolecules.

PL40
ONE HEALTH FOR TACKLING ANTIMICROBIAL RESISTANCE

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WHO CO of Türkiye

Antimicrobial Resistance (AMR) occurs when bacteria, viruses, fungi and parasites no longer respond to antimicrobial medicines. As a result of drug resistance, antibiotics and other antimicrobial medicines become ineffective and infections become difficult or impossible to treat, increasing the risk of disease spread, severe illness, disability and death.

AMR is a natural process that happens over time through genetic changes in pathogens. Its emergence and spread is accelerated by human activity, mainly the misuse and overuse of antimicrobials to treat, prevent or control infections in humans, animals and plants.

AMR is a complex problem that requires both sector-specific actions in the human health, food production, animal and environmental sectors, and a coordinated approach across these sectors. One Health refers to an integrated, unifying approach that aims to achieve optimal and sustainable health outcomes for people, animals and ecosystems. It recognizes that the health of humans, domestic and wild animals, plants and the wider environment are closely linked and inter-dependent. The One Health approach to preventing and controlling AMR brings together stakeholders from relevant sectors to communicate and work together in the design, implementation and monitoring of programmes, policies, legislation and research to mitigate AMR and attain better health and economic outcomes.

To coordinate the One Health global response to AMR, WHO works closely with the Food and Agriculture Organization of the United Nations (FAO), the UN Environment Programme (UNEP) and the World Organisation for Animal Health (WOAH). The 4 organizations (FAO, UNEP, WHO and WOAH) are known as the Quadripartite. A quadripartite joint secretariat is hosted by WHO to drive multi-stakeholder engagement in AMR. This has supported establishment of the Global Leaders Group on AMR, which began its work in November 2020, and the Multi-Stakeholder Partnership Platform, which was launched in November 2022, and several technical working groups.

The roadmap on antimicrobial resistance for the WHO European Region 2023-2030 was adopted on 26 October 2023 at the 73rd WHO Regional Committee for Europe in Astana, Kazakhstan with the aim of inspiring, guiding and supporting countries in the Region to identify, prioritize, implement and monitor high-impact interventions to tackle AMR, endorsed the Roadmap on antimicrobial resistance for the WHO European Region 2023–2030.

This roadmap is underpinned by inclusiveness, fostering broad partnerships and alliances and striving for greater representation of a diverse set of stakeholders and perspectives under the one health approach.

AMR has impacts for every sector, and every sector must be engaged in the response: the public and private sectors, across health, agriculture and environment

PL41
TOPICAL DRUG DELIVERY SYSTEMS FOR ANTIMICROBIAL PEPTIDES: ADVANTAGES AND CHALLENGES

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Introduction: Non-healing wounds and wound infections are a major problem for society due to significant burden to patients and high healthcare costs. As microbial biofilms are one of the main reasons for the development of non-healing skin wound infections, novel treatment strategies are sought to fight them. It has been shown that topical antimicrobial therapy has good potential as systemic side-effects can be avoided [1].

Natural antimicrobial peptides have been used by different living cells to shape the close vicinity of their production site. Antimicrobial peptides are good alternatives to antibiotics in fighting against pathogens. They eradicate the infections more effectively due to their mechanisms of action which is usually related to the direct damage of bacterial plasma membranes and/or penetration within the bacterial cytoplasm to access intracellular targets and cause rapid bacterial cell death [2]. Topical application of antimicrobial peptides is known to promote the migration of keratinocytes and fibroblasts, and this contributes significantly to an accelerated wound healing. Although there is huge potential in the application of different antimicrobial peptides in wound healing, they all face the same challenges: production, delivery and stability of the peptides *in vivo*.

The aim of our study was to design and develop novel wound dressings consisting of microfiber-encapsulated living bacterial cells by microfluidic electrospinning. Our goal was to investigate their potential to function as a drug delivery system for the *in situ* production of antimicrobial peptides and understand the advantages and challenges for this approach.

Materials and Methods: Microfluidic electrospinning was used to obtain living bacteria loaded fibrous wound dressings [3]. Formulation composition was varied in order to achieve reproducible electrospinning process and desired microfibrous structure of the dressings. Different probiotics (*L. plantarum, L. rhamnosus, L. lactis*) were used as model organisms to be used for the production of antimicrobial peptides. Scanning electron microscopy (SEM) analysis enabled us to visualize the morphology and reveal the fiber diameter changes. Confocal microscopy with SYTO9 and PI staining identified the locations of bacteria, their viability, and approximate concentration. Additionally, bacterial concentration and short-term storage stability were assessed under different environmental conditions (freezer vs room temperature). Antimicrobial efficacy was evaluated using a modified agar overlay assay and relevant wound pathogens such as *E. coli* DSM 1103, *S.aureus* DSM 2569, *P.aeruginosa* DSM 1117, *S.epidermidis* DSM 28319.

Results: Our developed method enabled the encapsulation of probiotic bacteria during *in situ* microfluidics electrospinning to enhance the viability of bacteria during and after electrospinning (**Figure 1**).

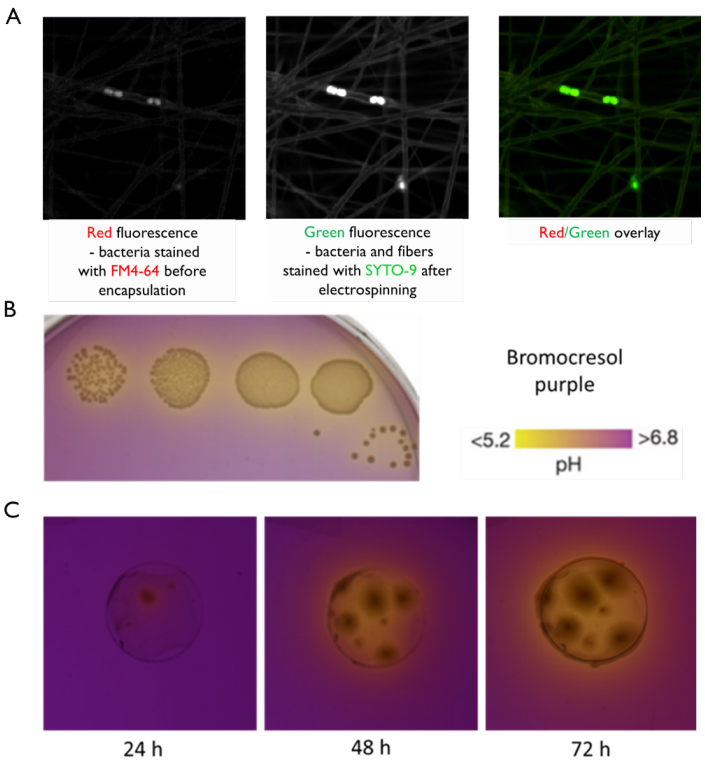

Figure 1. Schematics of in situ microfluidics electrospinning set-up.

SEM analysis revealed that homogeneous microfibers were obtained during electrospinning with no major electrospinning errors (e.g. beads). Electrospinning parameters and formulation required optimisation in order to achieve the best working conditions.

Different assays confirmed that porous microfibers allow two-way diffusion of substances through the nanopores on the fibres, and support the viability of entrapped bacteria. First, we showed that bacteria can be stained inside the microfiber dressing with fluorescent nucleic acid stain SYTO-9 (**Figure 2A**). Secondly, we used pH-sensitive dye bromocresol purple to monitor changes around microfiber dressing (**Figures 2B** and **C**). We saw that lactic acid bacteria within the microfiber dressings are able to metabolize and acidify the surrounding media.

All tested probiotics were successfully electrospun and the viability and functionality of bacteria preserved. The results revealed that the concentration of probiotics within the dressings was 106 cfu/cm2 (fibrous dressing of 1 mm thickness) and these probiotics preserved their antimicrobial activity during and after electrospinning within electrospun fiber dressings. Clear inhibition

zones were formed around the electrospun wound dressing consisting living probiotic bacteria against pathogenic wound bacteria. These results confirmed that the electrospun bacteria-loaded fiber dressing has potential to be used as a drug delivery system for wound healing.

Summary and Conclusions: We successfully developed probiotic-loaded fibrous drug delivery systems and characterized these and tested their in in vitro antimicrobial efficacy on relevant wound pathogens. It was shown that the composition as well as structure of the dressings affects their antimicrobial activity. The material will be further tested for antimicrobial efficacy in ex vivo infection models.

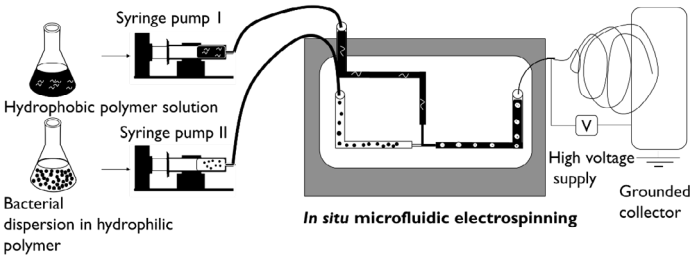

Figure 2. A - SYTO-9 staining of red fluorescent (FM4-64) bacteria inside fibers. L. lactis IL1403 grown on M17 + lactate+ 0.5% glucose agar with pH indicator. **B** – pure bacterial culture on agar plate. **C**- Circle disk of electrospun bacteria-containing fiber-dressing.

Acknowledgements: This study is supported by the Estonian Research Council grant no PRG1507. Probiotic strains were obtained from Bioprox (France) and TF-TAK (Estonia).

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ORAL PRESENTATIONS

OP001
NOVEL 4-NITRO-2-HYDROXYPHENYL-THIAZOL-HYDRAZONE HYBRIDS AND EVALUATION OF THEIR ANTI-NSLC PROFILES

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Introduction: Cancer is a general name for diseases affecting a single organ or the entire system. It causes the death of 100 to 300 out of 100,000 people in the world every year (1). Because of this major problem, in this study, novel twelve thiazole derivatives containing 4-nitro-2-hydroxyphenyl residue were designed and synthesized to test against A549 non-small lung cancer (NSCL).

Materials and Methods: The final compounds were caried out in three steps similar procedures (2). The structural analyzes of the compounds were made through NMR and HRMS techniques (3). Their anticancer activity profile was tested against A549 and L929 cell lines and apoptotic effects were examined via *in vitro* and *in silico* methods as same in previous study (1).

Results: The results indicated that the most active compound against cancer cells was **2j** (2-naphthyl), also it did not show cytotoxic effect against L929 healthy cells. However, the cytotoxicity of **2c** was not recorded on both cell lines. Additionally, methyl and methoxy groups have a significant impact positively on anticancer activity rather than fluoro, cyano, chloro, and nitro analogs. *In silico* results on caspase-3 enzyme indicated the stability of the complex was protected, therefor, compound **2j** activated caspase-3 enzyme.

Conclusions: Twelve thiazole derivatives were designed and synthesized with high yield. Their anticancer profiles were screened, and the results indicated that 4-nitro-2-hydroxyhydrazone-thiazole hybrids show good anticancer profile. Moreover, 2-napthyl analog (**2j**) was two times cytotoxic against A549 cells than cisplatin. Finally, this pharmacophore structure and the most active compound were marked as potential anticancer structures.

Acknowledgements: We thank Anadolu University BIBAM and Merkez laboratory for spectroscopic analyses.

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OP002
SYNTHESIS, MOLECULAR MODELLING STUDIES AND ANTICANCER ACTIVITY OF NOVEL PHENOTHIAZINE DERIVATIVES WITH CHOLINERGIC MODULATORY ACTION

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Introduction: Phenothiazines are anti-psychotics known to modulate cholinesterases while exhibiting cytotoxicity in liver cancer cells in vitro (1). In this study, several novel phenothiazine derivatives were synthesized. In silico AChE binding profiles, pharmacophore analysis and cytotoxic potential of these derivatives and commercial phenothiazines were investigated.

Materials and Methods: For the synthesis of intermediates (1-5), chloroacylchlorides in THF were added dropwise to the solution of appropriate phenothiazines and triethylamine in THF. Then the mixture was stirred until the starting materials were consumed. Synthesized intermediates were dissolved in THF and added dropwise to the mixture of corresponding amines and K2CO3, then heated under reflux until completion. After the synthesis, MTT assay was carried out against HCC cell lines (Human hepatoma cell line Hep3B, endothelial cell line SkHep1). Molecular docking, pharmacophore modelling and druglikeness estimation pipelines were done using Schrödinger Suite (2).

Results: Cytotoxic potential of the phenothiazine derivatives (1-28) revealed phenothiazine derivatives that are more active than the phenothiazine (PTZ) core. Moreover, in silico target screening and molecular docking analysis identified cholinesterases as the common targets of these phenothiazines. Compounds 1, 3, 8, PCP and TFP that were the most cytotoxic behaved similarly with Huprin W (HUW) interactions with the ACHE protein. Three of the most potent derivatives 1, 3 and 8 stabilized well in the binding site and gave the necessary interactions. Pharmacophore analysis showed us that 8, 9, 10 also possessed relatively higher fitness values.

Conclusions: Among the synthesized derivatives, the cytotoxic activity was the highest for 8 (R2=4-(2,3,4)-trimethoxybenzyl)-piperazine-1-yl). The intermediates 1 and 3 had -H and -SCH3 groups, respectively, at the 2nd position of the phenothiazine core. Among the novel derivatives, 8, 9, 10, and 25 had acetyl as linker group, leading to good IC50 values. These findings suggest that the substitution of the 2nd position of phenothiazine ring could be important when the linker is acetyl. These structural necessities were found to be important for the cytotoxicity of phenothiazine derivatives.

Acknowledgments: This study has been funded by The Scientific and Technological Research Council of Turkey (TUBITAK-116Z388) and the COST Action CA17112.

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OP003
DETERMINATION OF ANTIBACTERIAL AND ANTIBIOFILM ACTIVITY OF TERPINEN 4-OL AGAINST VARIOUS STANDARD BACTERIAL STRAINS

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Introduction: Antimicrobial resistance in bacteria is a significant public health problem. Biofilms are virulence factors that enable bacteria to tolerate environmental stressors and evade antibacterial agents. As a part of the defense mechanism of bacteria, biofilm makes the use of antibiotics ineffective in the treatment of infectious diseases. The inadequate treatment of diseases due to inappropriate and excessive use of antimicrobials has become a source of concern and has made the development of new agents vital. The use of natural agents as an alternative for treatment methods is an important and current solution strategy. Essential oils are among promising candidate for antibiotic-resistant bacterial and biofilm-associated infection treatments. Studies have shown that Melaleuca alternifolia essential oil, which contains terpinen-4-ol as its main active ingredient, exhibits antimicrobial activity against various Gram-positive and Gram-negative bacteria. The aim of this study was to investigate the antibacterial and antibiofilm activity of terpinen-4-ol against some standart bacterial strains.

Materials and Methods: Enterococcus faecalis WHO3 (vanA), Pseudomonas aeruginosa Pao-1 (biofilm producer strain), Staphylococcus aureus ATCC 43300 (MRSA), Staphylococcus epidermidis ATCC 35984 (biofilm producer strain), Streptococcus mutans ATCC 12575 (biofilm producer strain), and were used as test bacteria. The antibacterial activity of terpinen-4-ol was examined by broth microdilution method as the minimum inhibitory concentration according to European Committee on Antimicrobial Susceptibility Testing standarts. Crystal violet method was used to determine biofilm production and antibiofilm activity of terpinen-4-ol. Antibiofilm results were evaluated as percentage reduction.

Results: The MIC values of terpinen-4-ol were varied between 0.0625%-0.5% (v/v). Biofilm production of Pseudomonas aeruginosa Pao-1, Staphylococcus epidermidis ATCC 35984, Streptococcus mutans ATCC 12575 were 1,4362 ±0,047; 2,106 ±0,065; 3,054 ±0,414 and the biofilm inhibition of terpinen-4-ol at subMIC (MIC/2) concentrations were 79,95%; 77,79% and 73,23%, respectively.

Conclusions: The study found that terpinen-4-ol, the main active ingredient of TTO, has antibacterial and antibiofilm activity (biofilm producer strains) against standard test bacteria even at low concentrations. The potential use of terpinen-4-ol alone and in combination with various agents in the treatment and attenuation of pathogenic microorganisms should be supported by future studies.

OP004
FORMULATION OF AZACITIDINE-LOADED SERUM ALBUMIN NANOPARTICLES: IN-VITRO AND CYTOTOXIC EVALUATION

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Introduction: Leukemia describes a group of blood diseases characterized by the dysfunctional production and development of lymphocytes involved in body defence. The first treatment method for leukemia is chemotherapy. Azacitidine (AZA) is a hydrophilic chemotherapeutic for acute/chronic myelomonocytic leukemia that functions through the process of demethylation (1). The targeted delivery of therapeutics to tumour cells can be achieved by nanoparticles (NPs), which possess inherent permeability through blood vessels surrounding the tumour and restrict the exposure of healthy tissues to anticancer agents, and thereby toxicity (2). For targeted delivery, bovine serum albumin nanoparticles (BSA-NPs) have exhibited several benefits such as being biodegradable, biocompatible, and non-toxic/non-immunogenic (3). In this study, we aimed to prepare AZA-loaded BSA-NPs to decrease the treatment dosage of AZA for the treatment to eliminate the side effects.

Materials and Methods: AZA were obtained from Koçak-Farma (Turkey). Free and loaded BSA-NPs were prepared using the desolvation method. The effects of formulation variables on particle size (PS), distribution (PDI), and drug encapsulation (EE) were studied. AZA assay studies were carried out by HPLC (Agilent 1100, USA). Also, FT-IR analysis, zeta potentials, in vitro release rates, and cytotoxicity in HL60 cells were investigated.

Results: PS and PDI were found for free BSA-NPs between 97.8±0.10 to 619±3.93 nm and 0.05±0.02 to 1.0±0.01, respectively. Besides for AZA-loaded BSA-NPs, PS, PDI, and EE were found between 154.7±0.1 to 297.6±0.2 nm, 0.10±0.15 to 0.41±0.01 and 80.05%–99.93%, respectively. Zeta potentials were found between -33.92 and -41.63 mV. AZA showed a slow-release profile from NPs compared to free AZA. According to FT-IR studies, AZA was loaded into NPs. The IC50 was found at 5 µmol/L. The cell viability of NPs decreased with the increase in concentration.

Conclusions: The results revealed that the AZA-loaded BSA-NPs exhibited cytotoxic effects at decreased concentrations of AZA compared to free AZA. The results promise positive results for future studies.

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OP005
THE EFFECT OF INFILL PATTERN DESING AND AMOUNT OF BORIC ACID ON 3D PRINTED CHITOSAN FILMS

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Introduction: The aim of this study was to evaluate the effect of different infill patterns and the amount of Boric acid (BA) onto the characteristics of 3D printed chitosan films prepared by Semi-solid extrusion method (1). BA was used as a model drug due to its antimicrobial effect. The effect of formulation variables was evaluated by the design of experiment (DoE) approach with the Central Composite design (2). The film characteristics including thickness, degree of swelling, mechanical strength, adhesiveness, encapsulation efficiency and the percentage of drug released amount were output variables while the infill pattern and the amount of BA were input variables.

Materials and Methods: BA-loaded chitosan hydrogels were prepared by dissolving chitosan and BA in 1.5% (v/v) acetic acid at room temperature. Glycerol was used as plasticizer (25% w/w). The films were fabricated by an Axo A1 3D printer (Axolotl, Turkey). The amount of BA (X2) was increased from 10 mg to 30 mg gradually with different printing pattern (X1) (honeycomb (H), grid (G) and triangles (T)). The printing infill density of pattern and number of layers were 40% and 10 respectively. The film characteristics given above were evaluated also by microcomputed tomography (MicroCT).

Results: Films were prepared successfully with different infill patterns. In the response surface methodology results, the use of different patterns was significantly effective in the variables of thickness, adhesiveness, mechanical strength, swelling degree and the amount of BA released ($p<0.05$), while it was not found to be significant in the encapsulation efficiency ($p>0.05$). The highest thickness was obtained by G (423.33µm±22.51) and H (301.67µm±4.08), whereas the lowest thickness was obtained by T (206.67µm±19.66) pattern. The highest swelling degree, adhesiveness and mechanical strength was obtained by H-pattern, whereas the lowest values were observed by T-pattern. However, it was determined that the difference on the amount of BA and pattern variables had negative effect on the amount of BA released due to negative coefficient (-13.07*X1). While the degree of swelling and thickness increased, the released amount of BA decreased. The results of MicroCT analysis proved over 100% swelling degree due to 99% open porosity obtained for all formulations. Tissue integrity and high mechanical strength were verified by high connectivity (874) and anisotropy values (1.86) at the films prepared by H-pattern.

Conclusions: In this study, the data obtained from DoE showed that variations of pattern and amount of BA are effective on the characterization of films prepared by 3D printing. It has been proven that film formulation can be optimized with these variables.

Acknowledgements: This study was supported by a grant of TUBITAK (MAG-121R076)

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OP006
PRODUCTION AND CHARACTERIZATION OF BSA-LOADED PLGA NANOPARTICLES BY MICROFLUIDIC SYSTEM.

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Introduction: Biopharmaceutical products are vital in clinical therapy, yet maintaining their functionality poses challenges. Nanoparticulate systems offer promise for overcoming these delivery challenges, but traditional synthesis methods struggle with controlling particle attributes. Microfluidic systems provide precise control, enabling uniform nanoparticle preparation (Hamdallah et al., 2020). This study aims to produce poly(lactic-co-glycolic acid) (PLGA) nanoparticles via microfluidic chips, encapsulating bovine serum albumin (BSA), to evaluate their performance. This study aims to optimize particle attributes and identify optimal conditions for synthesizing protein-loaded nanoparticles through systematic experimentation and parameter optimization by adjusting parameters like total flow rate (TFR), flow rate ratio (FRR), and surfactant type.

Materials and Methods: The microfluidic chip was produced by Nehir Biotechnology (Ankara, Turkey). PLGA (lactide:glycolide 50:50) (Sigma-Aldrich, USA) was dissolved in acetone at ratios ranging from 1 to 5 mg/mL. BSA (Capricorn, Germany) was dissolved at concentrations ranging from 1 to 5 mg/mL in solutions of Pluronic®F-68 and Pluronic®F-127 (Sigma-Aldrich, USA) prepared at various concentrations. The syringes were connected to the microfluidic device. The oil and water phases were fed into the microfluidic device with various TFR and FRR using syringe pumps (NE-300) from two different inlets. The organic solvent of the collected solution was allowed to evaporate in a magnetic stirrer overnight (Roces, Christensen, & Perrie, 2020). The sizes of the NPs were evaluated using dynamic light scattering (DLS) (Zetasizer Ultra; Malvern Instruments, UK). The dialysis method was used for in vitro release studies.

Results: Promising results were obtained from BSA-loaded PLGA NPs produced by applying different fabrication parameters. NP structures with particle size between 140-196 nm and %encapsulation capacity between 23-90% were produced. Prolonged release of BSA was achieved with the optimized nanoparticle formulation.

Conclusions: In this study, an efficient procedure was obtained for BSA-loaded PLGA-NPs using a microfluidic method. This method is very promising for uniform nanoparticle preparation and encapsulation of different peptide/protein drugs.

Acknowledgments: This study received funding from the Ankara University Coordination Office for Scientific Research Projects (BAP) under grant TYL-2023-2894.

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OP007
BIOMIMETIC DRUG DELIVERY SYSTEMS: FORMULATION AND CHARACTERIZATION OF ADIPOSE STEM CELL MEMBRANE-COATED CHITOSAN NANOPARTICLES

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Introduction: In recent years biomimetic drug delivery systems, prepared based on the idea that the body's complex barriers can only be overcome by using the body's natural components, have come to the fore. (1) These systems combine both the properties of natural cells and the advantages of synthetic nanoparticles. (2) Our study aims to develop biomimetic chitosan nanoparticles carrying teriflunomide (TRF) by utilizing adipose stem cell membranes for the treatment of Multiple Sclerosis (MS).

Materials and Methods: TRF-loaded chitosan nanoparticles were prepared by solvent evaporation method and optimized with the help of artificial intelligence, following QbD process steps. The biomimetic cell membrane ghost structure was isolated from adipose stem cells with the help of different hypotonic lysis buffers and homogenization techniques. In further steps, various incubation techniques were employed to coat the ghost structure around nanoparticles. After the characterization studies on different nanoparticles based on the particle size and zeta potential measurements, the final biomimetic system was further evaluated in stability studies, TEM, and BSA-model protein analysis.

Results: The particle size and zeta potential of the optimum TRF-loaded chitosan nanoparticle was 228.3 nm and +29.9 mV, respectively. High pressure homogenization followed by mechanical mixing gave the optimum biomimetic formulation with a particle size of 239.6 nm and zeta potential of +22.2 mV. The cell membrane coating on the surface of nanoparticles was shown by TEM analysis. Overall change in particle size and zeta potential values, BSA analysis results, and TEM images revealed the formation of biomimetic nanoparticles.

Conclusions: As a result, biomimetic nanoparticle formulations were prepared successfully. It is thought that biomimetic formulations will be an innovative strategy in the treatment of MS.

Acknowledgements: This study was supported by TUBITAK under grant SBAG-121S478. The authors would like to thank Olon S.p.A. (Italy) for providing TRF.

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OP008

A NEW FLAVONE HETEROSIDE AND TERPENOIDS FROM SCORZONERA HIERACIIFOLIA, AN ENDEMIC SPECIES FROM TÜRKİYE.

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Introduction: The isolation and evaluation of the biological activity of naturally occurring compounds is one of the major topics in pharmaceutical sciences. The genus Scorzonera has approximately 180 species in the world and 52 species, 31 of which are endemic, grow naturally in Turkey. Scorzonera L. species have been reported to be consumed as food and used in traditional medicine (1,2). Phytochemical studies on Scorzonera species revealed that the genus is rich in flavonoids, dihydroisocoumarins, triterpenes and sesquiterpenes (3,4). As part of an ongoing study on the Scorzonera genus, a phytochemical analysis was conducted on Scorzonera hieraciifolia species grown in Turkey.

Materials and Methods: S. hieraciifolia was collected from Konya in June 2009 [Herbarium No: Makbul 127 & Çoşkunçelebi (RUB)]. The underground tubers of the plant were extracted with methanol according to the maceration method and the crude methanol extract was fractionated with n-hexane, dichloromethane, n-butanol, and water. Chromatographic separation of n-hexane and n-butanol fractions of the crude methanol extract obtained from the underground tubers of S. hieraciifolia led to the isolation of 6 pure compounds.

Results: A total of 6 compounds from the n-hexane and n-butanol fractions of S. hieraciifolia; three triterpenes (taraxasterol, pseudotaraxasterol and taraxasterol-3-O-β-acetate), a new flavone heteroside (scorzohiearacoside), carbohydrate (sucrose), and 1-octadecene were isolated by various chromatographic methods. Their structures have been elucidated and ascertained spectroscopically (NMR 1H, 13C, COSY, HMBC, HSQC, and LC-QTOF-MS).

Conclusions: Scorzohiearacoside, a novel flavonoside, was detected for the first time in this study. All other compounds were isolated from S. hieraciifolia for the first time. The isolated pure compounds have the potential to contribute both to the chemotaxonomy of the genus and to drug discovery studies with pharmacological activity studies to be carried out on the compounds to be isolated.

Acknowledgements: This study was supported by Karadeniz Technical University of KTU-BAP (Project No. TSA-2020-8961)

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OP009
A NOVEL NORMONOTERPENE GLYCOSIDE AND TWO NEW BENZOPHENONE GLYCOSIDES FROM HYPERICUM CERASTIOIDES (SPACH) N.ROBSON

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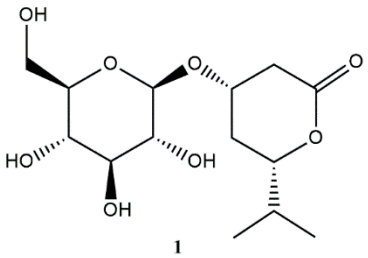
Introduction: The Hypericum genus comprises more than 500 species widely distributed throughout the world (1). Extracts and isolates derived from different Hypericum species were shown to possess antibacterial, anti-inflammatory, antioxidant, antihyperglycemic, and cytotoxic activities (2,3). Previous phytochemical studies on different Hypericum species revealed the presence of naphthodianthrones, phloroglucinols, xanthones, flavonoids, and benzophenones (2,3). This study aims to isolate secondary metabolites from H. cerastioides with potential bioactivity.

Materials and Methods: The aerial parts of H. cerastioides were collected from İstanbul in 2023. The plant materials were extracted with EtOH. The crude extract was suspended in water and then partitioned against petroleum ether, ethyl acetate, and n-butanol. Polyamide, MPLC, and Sephadex LH-20 CCs were used for the isolation of compounds from petroleum ether and ethyl acetate fractions. The chemical structures of the isolates were determined by 1D and 2D NMR experiments as well as HRMS analysis.

Results: A novel normonoterpene glycoside (1), and two new benzophenone glycosides (2 and 3) were isolated along with ten known secondary metabolites. The known compounds were identified as daucosterol linoleate, garcimangosone D, chlorogenic acid, epicatechin, 1,7-dihydroxy-5,6-dimethoxy xanthone, 6-O-p-coumaroyl-α/β-glucopyranose, rutin, isoquercitrin, I3-II8-biapigenin and quercetin.



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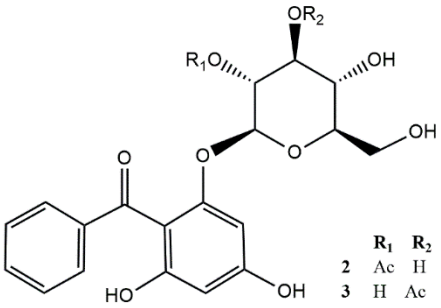

Conclusions: A novel normonoterpene glycoside and two new benzophenones were obtained from H. cerastioides. In addition, all compounds except for rutin are being reported from this species for the first time. The in vitro cytotoxicity evaluation of the isolates is underway in our laboratory.

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OP010
TOTAL PHENOLIC CONTENT AND ANTIOXIDANT ACTIVITY OF THE ROOTS OF ROSA CANINA L. AND ISOLATION OF THE MAIN COMPOUNDS.

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Introduction: The roots of Rosa canina L. are used in folk medicine for ailments such as dyspnea, colds, asthma, diabetes, hemorrhoids and rheumatism (1,2). This study aimed to isolate the major compounds from the roots of R. canina, to investigate the antioxidant activities of the extracts prepared from the roots and the isolated compounds, as well as the total phenolic content of the extracts.

Materials and Methods: The isolation studies were carried out on the subextracts prepared from the methanol extract using various chromatographic methods. The structure of the isolated compounds was determined with the help of 1D and 2D NMR spectral techniques. The antioxidant activity of the methanol extract, subextracts (chloroform, ethyl acetate, remaining aqueous), and isolated compounds was determined by Ferric-Reducing Antioxidant Power (FRAP) and Cupric Ion Reducing Antioxidant Capacity (CUPRAC) assays. In addition, the total phenolic content of the extracts was examined by the Folin-Ciocalteu method.

Results: The isolation studies led to the purification of catechin (1), 2α,3β,19α-trihydroxyurs-12-en-28-O-β-D-glucopyranoside (2), 2-oxo-pomolic acid (3), and kaji-ichigoside F1 (4) from the ethyl acetate subextract, tormentic acid (5) and euscaphic acid (6) from the chloroform subextract. In FRAP assay, the chloroform subextract (1796.733 ± 3.859 µM Trolox equivalents (TE)/g) and in CUPRAC assay, the ethyl acetate subextract (930.000 ± 0.900 µM TE/g) exhibited the highest antioxidant activity. Catechin was the compound that showed the highest potency in both assays (FRAP = 1711.733 ± 0.956, CUPRAC = 1044.028 ± 1.039 µM TE/g). It was determined that the remaining aqueous subextract had higher total phenolic content (698.708 ± 3.680 GAE µg/mL) compared to the other extracts.

Conclusions: The results of the study revealed the antioxidant potential of R. canina and its isolated compounds, and it is thought that its roots may be a natural source of antioxidants.

Acknowledgements: This study was supported by a grant of TUBITAK (1919B012337704) and Scientific Research Projects Coordination Unit of Karadeniz Technical University (Project number: TLÖ-2023-11098).

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OP011
PHENOLIC CONTENT AND ANTIFUNGAL ACTIVITIES OF GREEN TEA AND MATCHA TEA PRODUCTS.

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Introduction: Camellia sinensis (L.) Kuntze, consumed as a tea form, is considered one of the most important functional foods due to its positive effects on health (1). The unfermented green tea exhibits direct or indirect antimicrobial effects against bacteria, viruses, and fungal agents (2). In this study, we determined the phenolic compounds of green tea and Matcha tea samples and some of their dietary supplements. In addition, the antifungal activity of these samples against the Yeast-type fungi called Candida sp., defined as opportunistic fungi that can cause localized and invasive infections (3), was investigated.

Materials and Methods: In the study, the phenolic compounds of 15 products were analysed using the LC-ESI-MS/MS. The antifungal activity against Candida strains of lyophilised aqueous extracts prepared from green tea and Matcha tea samples was also examined.

Results: The phenolic contents of green tea samples and food supplements were determined by the LC-ESI-MS/MS method. The phenolic components in tea and their food supplements were analyzed using the LC-ESI-MS/MS method and be qualitatively compatible with the literature data. Still, quantitatively, the phenolic compounds detected in the products varied. In our study, the antifungal effect was observed in all green tea samples but not in the extracts except for three samples of Matcha tea. In addition, it was observed for the first time in our study that Matcha tea had an antifungal effect against C. glabrata and C. parapsilosis.

Conclusions: Our results suggest that green tea and Matcha tea may be effective adjuvant treatments against Candida sp. It can also be used prophylactically in people suffering from immune system deficiency, which may be helpful considering the literature data and our results.

Acknowledgments: Declared none.

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OP012
ANTIOXIDANT AND ANTIMICROBIAL PROPERTIES OF SELECTED PHARMACY ORIGINATED MEDICINAL PLANTS

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Introduction: Ethnobotanical uses of medicinal plants have always been a good starting point for pharmacognosy research. Majority of the papers on activity of medicinal plants, especially antioxidant and antimicrobial activities, investigation of medicinal plants generally made on plants obtained from herbal markets or wild plants. Along with their highly beneficial health properties medicinal plants should be used under qualified supervision and with correct, high quality plant material. The aim of this study determination of antimicrobial and antioxidant properties of selected medicinal plants, obtained from a company that only provides to pharmacies in Turkey. Those medicinal plants were selected according to their ethnobotanical uses against infections (1-4).

Materials and Methods: Lavandula intermedia, Vitis vinifera, Crataegus sp. and Capparis ovata were obtained from a company that sells only to pharmacies and has an organic agriculture certificate. The extracts of the plants were obtained by infusion method with ethanol:water (1:1) and water and subjected to investigation for antioxidant and antimicrobial activities. The extracts were investigated for their antioxidant capacities using DPPH radical scavenging activity method and CUPRAC assay. The total phenol content (TPC) was spectrophotometrically determined with Folin-Ciocalteau Reagent. The extracts of the plants were evaluated for their antimicrobial activity against various bacterial and fungal strains by microdilution method, and Minimum Inhibitory Concentration (MIC, µg/mL) values were determined.

Results: The results showed that the ethanolic water extract of Vitis vinifera exhibited the highest antioxidant activity with DPPH radical scavenging activity (IC50: 0,011±0,005 mg/mL), CUPRAC (0,829±0,051 mM trolox/mg extract) and TPC results (0,107±0,016 mg GAE/mg extract) than the other extracts of plants. The highest antimicrobial activity was observed in ethanolic water extract of V. vinifera against Staphylococcus epidermidis (MIC=78,12 µg/mL), Candida parapsilosis (MIC=156,25 µg/mL) and Candida tropicalis (MIC=156,25 µg/mL) strains.

Conclusions: Ethanolic water extract of Vitis vinifera showed highest antioxidant and antimicrobial activity amoung the tested medicinal extracts. Due to the fact that not all chemical compounds in medicinal drugs are soluble in water, the difference between the activity results of water and ethanolic water extracts of V. vinifera was observed.

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OP013
DESIGNING THE MOLECULARLY IMPRINTED POLYMER-BASED ELECTROCHEMICAL SENSOR FOR THE DETERMINATION OF DOBUTAMINE

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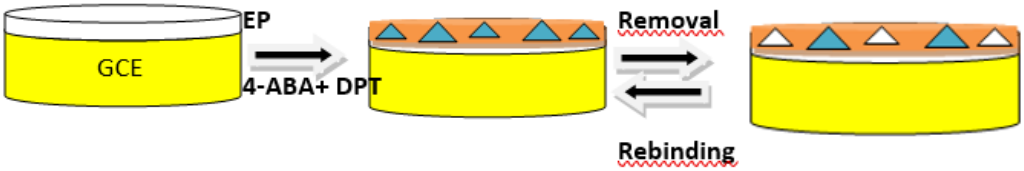
Introduction: Dobutamine (DBT), is an inotropic synthetic catecholamine with a strong β-adrenergic activity(1). DBT is a medication used in the treatment of cardiogenic shock (as a result of inadequate tissue perfusion) and severe heart failure(2). MIPs are structures with cavities specifically designed for the target molecule using various polymerization techniques. In addition to the template molecule and the appropriate functional monomer, polymerization is performed in the presence of other components (Scheme 1). The extraction of the template molecule by removal results in the formation of compatible cavities in terms of shape, structure, and functional groups, thus enabling selective recognition. As artificial receptors, MIP-based sensors recognize the analyte, which is detected at a low level (pM, fM).



Scheme 1. The fabrication of MIP film and rebinding/removal process

This study aims to determine the DBT using a developed MIP-based electrochemical sensor. The polymeric film was formed by electropolymerization on the glassy carbon electrode (GCE).

Materials and Methods: All electrochemical measurements were performed with an IVIUM compactstat potentiostat (Eindhoven,

Before modification of the electrode surface, the GCE surface was thoroughly cleaned with alumina in the polish pad. The GCE was passed through the distilled water and methanol. To prepare the polymeric film solution, 0.2 mM DBT and 0.6 mM 4-ABA were mixed as a 1:3 ratio (v/v) in the pH 7.0 phosphate buffer. The GCE was electropolymerized in a polymeric film solution by scanning the potential with CV between –0.2 and 1.5 V. To obtain the cavity in the polymeric matrix, the GCE was immersed in the removal solution(pH 10.5 phosphate buffer), and the CV was performed by scanning the potential between –2.0 and 1.5 V. To control the MIP sensor, the NIP sensor was formed using the same fabrication protocol without the analyte.

The characterization and analytical performance of MIP and NIP sensors were evaluated by the CV and DPV with the redox probe, 5 mM $[Fe(CN)_6]^{3-/4-}$ and were compared.

Results: Surface and electrochemical characterization of the 4-ABA@MIP/GCE sensor have been done. After screening and optimization studies were carried out to fabricate an MIP-based electrochemical sensor, the analytical performance of 4-ABA@MIP/GCE and the validation parameters were tested according to the ICH guidelines. Specificity/selectivity of the developed sensor has been shown by using common interferents found in the biological fluids and also molecules having similar structures, such as dopamine, levodopa, and carbidopa.

Conclusions: The 4-ABA@MIP/GCE is the first electrochemical sensor developed to determine DBT. A quantitative analysis method has been developed and validated by using the 4-ABA@MIP/GCE sensor in the concentration range of 0.1–1.0 pM. The method's applicability has been shown for commercial serum samples with good recovery and RSD% results.

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OP014
EXHAUSTIVE APPROACHES FOR THE INTERACTIONS OF AN ANTIHIPERTANSIVE DRUG MACITENTAN WITH BOVINE SERUM ALBUMIN

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Introduction: Treatment for symptomatic pulmonary arterial disease involves the administration of the endothelial receptor antagonist drug macitentan (MACI). (1) Macitentan's approval as an endothelial receptor antagonist has increased the number of patients treated for hypertension; nonetheless, the interaction of the drug with blood proteins plays a crucial role in the therapeutic usage of this medication. (2) In order to fully understand the impact of macitentan on human health, it is crucial to elucidate its interaction with plasma proteins.

Materials and Methods: In this research, several spectroscopic techniques and computations, including fluorescence and UV-vis absorption, were used to explore the interaction between MACI and bovine serum albumin (BSA) and it was confirmed with electrochemical study.

Results: The MACI-BSA complex was created by MACI by a dynamic method that quenched the fluorescence of BSA. The increase in ka value with temperature also confirms that the interaction is a dynamic interaction. (3) This drug exhibits a moderate binding strength to BSA, as evidenced by the binding constant of 1,27-7,25 x 104 M-1 when the MACI-BSA interaction was investigated.

Conclusions: The MACI-BSA complex appeared to form spontaneously as a result of hydrophobic interactions, van der Waals interactions, and hydrogen bonds when the thermodynamic results were analyzed. (4) It was discovered using synchronous and three-dimensional fluorescence investigations that the environment surrounding the tryptophan and tyrosine residues of BSA changed when MACI was integrated into the protein. Also, the interaction between the drug and BSA was confirmed with electrochemical study.

Acknowledgements: Selenay Sadak thanks the financial support from The Scientific and Technological Research Council of Turkey (TUBITAK) under the BIDEB/2210-A master's scholarship programme.

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OP015

A NOVEL GREEN AND ECO-FRIENDLY UPLC METHOD FOR THE QUANTIFICATION OF EDOXABAN AND METOPROLOL TARTRATE IN HUMAN PLASMA AND URINE SAMPLES: AN ASSESSMENT OF THE GREENNESS PROFILE OF THE DEVELOPED METHOD WITH AN ANALYTICAL ECO-SCALE, NEMI, GAPI AND AGREE

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Introduction: Edoxaban (EDO) is a direct factor Xa inhibitor, which belongs to the group of direct oral anticoagulants (DOACs). EDO was recently approved in the United States and Japan for prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation and for treatment of venous thromboembolism, and secondary prevention of arterial ischemia in patients with chronic coronary or peripheral arterial disease [1].

Metoprolol1 is a β1-selective adrenoceptor blocking drug. It is similar in efficacy to other β-adrenoceptor blocking drugs in angina pectoris and essential hypertension, when given in equative β-blocking dosages [2]. Metoprolol is commercialized as tartrate salt (METO), which is used with or without other medications to treat high blood pressure (hypertension).

In Turkey, Edoxaban and Metoprolol Tartrate are often prescribed together to prevent possible heart attack risks and heart rhythm disturbances. This study was carried out to develop a new UPLC method for quantitative determination of EDO and METO in biological samples.

Materials and Method: Chromatographic analyses were performed in isocratic mode, and efavirenz was found as a suitable internal standard. A Waters Acquity UPLC® HSS T3 column (1,8 µm, 2,1 mm X 100 mm) was used as stationary phase, pumping the mobile phase (methanol:water (70:30 *v/v*)) at the rate of 0.3 mL/min. Analytical method validation was performed according to ICHQ2(R1) guideline. Plasma proteins were precipitated with acetonitrile at a ratio of 1 volume sample to 2 volumes acetonitrile. All solutions were vortexed and centrifuged, then clear supernatants were separated and filtered before analysis. Urine samples was prepared liquid-liquid extraction.

Results: The linearity ranges were found to be between 1,25 µg/mL and 12,5 µg/mL for EDO and 1,1 µg/mL and 11 µg/mL for METO. The analysis time was under 6.5 minutes. The retention times of EDO, METO and EFA are 2.2 min, 3.08 min, 5.11 min, respectively, and the recovery is over 95% in human plasma and urine samples. The greenness profile of the developed method was evaluated with analytical eco-scale, NEMI, GAPI and AGREE.

Conclusions: A new UPLC approach for determination of EDO and METO was successfully developed and validated. The method possesses sufficient sensitivity for the quantitative determination of EDO and METO in plasma and urine samples.

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OP016
PRODUCTION OF A NANOMATERIAL-SUPPORTED MOLECULARLY IMPRINTED POLYMER-BASED ELECTROCHEMICAL SENSOR FOR SELECTIVE AND RAPID QUANTITATIVE DETECTION OF GLIMEPIRIDE

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Introduction: Glimepiride (GLP), a modern oral hypoglycemic drug, is a member of the sulfonylurea derivative group (1). This study was designed by combining the excellent conductivity, electrocatalytic activity and stability properties of selected nanomaterials (multi-walled carbon nanotubes functionalized carboxylate (MWCNT-COOH), multi-walled carbon nanotubes (MWCNT), and zinc oxide nanoparticle (ZnONPs)) with the affordable price, good sensitivity, easy application, and environmentally friendly properties of molecularly imprinted polymer (MIP) based electrochemical. 2-Acrylamido-2-methyl-1-propanesulfonic acid (AMPS) was used as the functional monomer along with other MIP components. This study describes the design, characterization, and validation of a nanomaterial-doped MIP-based electrochemical sensor (AMPS/MWCNT-COOH@ZnONPs-MIP/GCE) for GLP determination.

Materials and Methods: GLP was prepared as 1.0 mM stock solution in methanol. NOVA 2.1.5 software on AUTOLAB was used as a potentiostat for electrochemical measurements. Before preparing the photopolymerization solution, 1 mg of all nanomaterials was taken, and dispersed in 1 mL DMF and kept in an ultrasonic bath for 2 hours. 20 µL of each solution- GLP (1.0 mM) and AMPS (1.0 mM)- were mixed by vortexing for 1 min in a 2 mL Eppendorf tube. 20 µL of 1:1 mixture of MWCT-COOH: ZnONPs was added to this mixture and kept in an ultrasonic bath for 15 min. 80 µL HEMA and 16 µL EGDMA were added, and the mixture was vortexed again for 1 min. 20 µL of the resulting mixture was taken into another Eppendorf tube, and 2 µL of initiator was added. A volume of 0.5 µL was taken from this solution and dropped onto the GCE surface. The sensor was kept under 365 nm and 100W UV light for 5 min for the photopolymerization process. The sensor was made ready for use in the next stages.

Results: The fabricated sensor was characterized by means of scanning electron microscopy (SEM), electrochemical impedance spectroscopy (EIS), X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR), energy dispersive X-ray analysis (EDX), and cyclic voltammetry (CV). The indirect measurements using 5.0 mM [Fe(CN)6]3–/4—solution were used to determine GLP in the linear range of 2.5–17.5 pM. For standard solutions, the limit of detection (LOD) and limit of quantification (LOQ) were obtained as 0.42 pM and 1.40 pM, respectively. The GLP recovery values for the tablet form and commercial serum samples were calculated as 101.82% and 101.19%, respectively.

Conclusions: In this research, the first electrochemical application of the MIP-based modified sensor for GLP detection was presented. The sensor was successfully applied to tablet form and commercial serum samples and exhibited high selectivity, sensitivity, low cost, simple procedure, and stability. The designed sensor showed high selectivity in detecting GLP even in the presence of interfering agents at levels 10-fold higher than those found in body fluids. The selectivity study was performed using model drugs comparable in structure and chemistry.

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OP017
MACRO AND TRACE ELEMENT LEVELS FOLLOWING INTRACEREBROVENTRICULAR CANNULA AND DEXMEDETOMIDINE INJECTION IN GENETIC ABSENCE EPILEPSY RATS

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Introduction: Recent reports show that the etiology of absence epilepsy may be significantly influenced by trace elements1,2. This study aim to investigate the accumulation of trace elements in the brains of Genetic Absence Epilepsy Rat from Strasbourg (GAERS) during absence status epilepticus induced by the activation of specific alpha-2a adrenergic receptors (α2AAR) via intracerebroventricular injection of dexmedetomidine (DEX)3.

Materials and Methods: A total of adult 15 male GAERS used. Stereotaxic surgery was performed to implant electrodes on the frontoparietal cortices and a guide cannula into the lateral ventricle. The rats were grouped as GAERS-naïve (n=5), GAERS injected with saline (GAERS-SAL; n=4), and GAERS injected with DEX (GAERS-DEX; n=6). In order to induce absence status, DEX was through intracerebroventricular route. After the induction of the second period of the absence statuses, rats were sacrificed. Cortices and hippocampi were isolated and macro/trace metals were analyzed using inductively coupled plasma mass spectrometry (ICP-MS), the levels of several trace elements quantified. Unpaired t-test was used to analyze the differences between the groups.

Results: In the cortex and hippocampus, 25Mg, 55Mn, 57Fe, 88Sr, 65Cu, 42Mo, 80Hg, 15P, 52Cr, 59Co, 66Zn, 82Se, 85Rb, 133Cs, and 205Tl; in the hippocampus additionally 43Ca were statistically higher in the GAERS-NAIVE group in comparison to GAERS-SAL ($p < 0.05$). On the other hand, no significant differences were observed between the GAERS-SAL and GAERS-DEX groups.

Conclusions: Our results indicate that absence status induced by DEX does not affect trace element levels in the cortex and hippocampus, unlike convulsive forms of epilepsy. Interestingly, the placement of cannulas seemed to impact trace element levels, raising questions about the current methodology of intracerebroventricular cannula placement.

Acknowledgements: This study was supported with the travel grant from Kerem Aydinlar Vakfi.

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OP018
DEVELOPMENT AND IN VITRO EVALUATION OF MESALAZINE AND CHITOSAN/TNF-A SIRNA POLYPLEX LOADED SILK FIBROIN-BASED HYDROGELS BY 3D BIOPRINTING

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Introduction: Inflammatory bowel disease (IBD) is a chronic disease manifested by chronic diarrhea, bleeding, and abdominal pain due to ulceration of the colon or rectum (1). The aim of this study is to develop and investigate 3D printed silk fibroin-based hydrogels loaded mesalazine and chitosan/TNF-α siRNA polyplex for oral use in IBD.

Materials and Methods: Silk fibroin was produced from silkworm cocoons. Silk fibroin, sodium alginate and hyaluronic acid based bioink formulations were prepared and optimized by viscosity, surface tension and printability measurements. Then, optimum chitosan/TNF-α siRNA polyplex was determined. After loading of mesalazine and chitosan/TNF-α siRNA polyplex to optimum bioink formulation, oral hydrogel formulation was bioprinted with 3D bioprinter. Differential scanning calorimetry (DSC), Fourier transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), thermogravimetric analysis (TGA), mechanical, morphological analysis, in vitro degradation, swelling index, mucoadhesion and in vitro dissolution studies were carried out within the scope of in vitro characterization studies.

Results: Mesalazine and chitosan/TNF-alpha siRNA polyplex loaded silk fibroin based oral hydrogel formulation was successfully prepared by 3D printing technology. No peak or pattern of mesalazine was seen in the XRD, DSC and FTIR analysis of hydrogel. TGA results showed that the hydrogel lost weight depending on the temperature. It was found that approximately 30% of the hydrogel was degraded over 24 hours and had a swelling capacity of approximately 400%. In morphological analysis, it was observed that the hydrogel had a cloudy and homogeneous structure, while the lyophilized hydrogel had a porous structure. Hydrogel had mechanical strength suitable for oral use and showed mucoadhesion onto colonic tissue. Controlled release of mesalazine and TNF-α siRNA was obtained for 24 hours, with the hydrogel developed.

Conclusion: It was concluded that the 3D bioprinted silk fibroin-based oral hydrogel loaded with mesalazine and chitosan/TNF-α siRNA polyplex has a potential for oral treatment of IBD.

Acknowledgement: This study was supported by Gazi University Scientific Research Projects Coordination Unit under grant number 02/2020–20.

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OP019
PREPARATION AND IN VITRO CHARACTERIZATION OF QUERCETIN LOADED PHYTOSOMES

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Introduction: Quercetin is a phyto-active compound with remarkable pharmacological potential, however it has limited oral bioavailability. In order to increase its absorbtion through gastro-intestinal system many strategies have been examined by means of various drug delivery systems (1). Phytosomes can be given as an example for phospholipid-based carriers among these delivery systems. The aim of this study was to demonstrate the characterization of quercetin loaded phytosomes in in vitro conditions.

Materials and Methods: Quercetin and L-α-Phosphatidylcholine (PC) from egg yolk were purchased from Sigma. Solvent evaporation/thin film formation method was used to prepare phytosomes (2). Quercetin phospholipid ratios, process temperature (40, 50, 60 oC) and reaction time (1,2,3 h) were used as formulation parameters. In order to characterize the formulations, encapsulation efficiency (EE%), particle size, polydispersity index and zeta potential were determined. In direct method was used for the determination of entrapment efficiency. Among all the prepared formulas, the three formulas with the highest loading efficiency were chosen (Table 1). X-ray Diffraction (XRD) of these formulations was determined

Results: In the formulations as the PC ratios increased, particle size and PDI values decreased, but EE% increased. ZPs were independent. The absence of a Quercetin peak for XRD results indicates that there was an amorphous structure of the active ingredient in the formulation and phytosome structure formed. The results of the formulations were shown in Table 1.

Table 1. Formulations parameters and results

Q:PC ratio	Temperature (oC)	Reaction time(h)	EE(%)	Particle size (nm±SD*)	PDI±SD*	ZP (mV±SD*)
1:2	50	2	79,01	1209±18,00	28,6±0,056	28,6±0,056
1:2,25	50	2	86,96	1006±24,22	26,5±0,057	26,5±0,057
1:2,5	50	2	88,21	839±12,78	27,2±0,929	27,2±0,929

*Standart Deviation, n=3

Conclusion: To conclude, the prepared phytosome formulations were found very promising for the oral delivery of Quercetin.

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OP020
ANTIMICROBIAL NANOCLAYS DOPED MICROPARTICLES FOR ENHANCED WOUND HEALING

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Introduction: In chronic wounds, as venous leg ulcers, arterial ulcers, diabetic ulcers, and pressure ulcers, the healing process does not lead to anatomical and functional recovery (1). Given these premises, the aim of this study was the design and the development of chitosan-based microparticles loaded with Cu2+-doped-clay minerals as a powder for cutaneous application to enhance the healing and prevent infections in chronic wounds. To compare natural and synthetic clay, two clays were used: the natural clay was a montmorillonite (MMT), while the synthetic one was a layered double hydroxide (LDH).

Materials and Methods: The Cu-based MMT was prepared by means of an intercalation solution procedure, while the Cu-based LDH was obtained through the coprecipitation method. Solid-state characterizations were performed. Chitosan carbamate was prepared by adding NH4HCO3 to a chitosan acetate salt solution (2). Then, Cu2+-MMT or Cu2+-LDH were added to the chitosan carbamate aqueous blends. The microparticles were obtained by means of a Mini Spray-Dryer (Buchi 190) and characterized by physico-chemical properties (morphology, size distribution, solid state, and thermal profiles). Moreover, preclinical in vitro properties (cytocompatibility, fibroblasts adhesion and proliferation, in vitro wound healing, antimicrobial assay, and in vivo evaluation on a murine model) were assessed.

Results: The microparticles were obtained starting from a chitosan derivative, chitosan carbamate, which was successfully synthesized. Aqueous solutions of chitosan carbamate were useful to preserve the clay structure by eliminating the acidic conditions which are necessary for the solubility of chitosan. All the spray-dried microparticles were characterized by spherical and smooth morphology and preserved their structures upon hydration independently of their composition. The physico-chemical characterizations confirmed the successful loading of Cu2+-clays in the microparticles. In addition to the enhanced cell proliferation together with haemostatic properties, the presence of Cu2+-clays boosted the microparticles' antibacterial properties. The preclinical in vivo results demonstrated to promote skin tissue repair in a murine model.

Conclusions: The preclinical in vitro and in vivo encouraging results revealed that these biomimetic microparticles doped with Cu based clay minerals could be considered promising candidates to simultaneously enhance the healing and control infections in chronic wounds.

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OP021
THE EFFECT OF MAGNETIC SCAFFOLDS AND MECHANOSTIMULATION ON TENDON REGENERATION

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Introduction: Tendon pathologies are medical conditions accompanied by inflammatory and degenerative alterations, such as tendinopathies and tendinitis. The aim of the present work was the development of fibrous scaffolds based on polyhydroxybutyrate (PHB) doped with magnetic iron oxide nanoparticles (Fe3O4 NPs) and coated with gelatin (Gel), able to mimic the hierarchical structure of the tendon and to improve the tissue healing potential [1,2].

Materials and Methods: The blends were spun using a centrifugal spinning apparatus obtaining PHB, PHB-Fe3O4, and PHB-Fe3O4-Gel fibers. The systems morphology and the surface wettability were evaluated. The scaffolds' superparamagnetic behavior, mechanical properties and weight loss in physiological medium were evaluated. Finally, cell adhesion and proliferation in vitro were evaluated with and without the application of static magnetic fields of different extent for 21 days of culture.

Results: The systems were characterized by an aligned structure and Fe3O4 NPs were successfully incorporated into the fibrous structure, increasing the scaffolds' rigidity. Moreover, the presence of Gel increased the surface wettability. PHB-Fe3O4 and PHB-Fe3O4-Gel were characterized by a superparamagnetic behavior, while the PHB scaffold was characterized by a spectrum typical of not-magnetic samples. The scaffolds showed a progressive weight loss in physiological medium, while maintaining the fibers' morphology and alignment for 3 months. Finally, the application of the magnetic fields led to a significant increase in cell proliferation, and alignment onto the systems loaded with magnetite, mimicking the tendon fascicles.

Conclusions: Fibrous scaffolds based on PHB and Gel and doped with magnetite were successfully manufactured, representing an interesting tool to enhance the wound regeneration when combined with the application of external magnetic fields.

Acknowledgements: EB wishes to thank the project NODES (MUR – M4C2 1.5 of PNRR funded by the European Union - NextGenerationEU (Grant agreement no. ECS00000036) for funding the Post Doc grant

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OP022
GOLD NANOPARTICLE-FUNCTIONALIZED PACLITAXEL-LOADED NANOCARRIERS FOR ENHANCING ANTICANCER EFFICACY THROUGH CHEMO-PHOTOTHERMAL THERAPY.

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Introduction: Nanocarrier systems containing chemotherapeutics (CTs) constitute an important part of modern cancer treatment. However, many obstacles limiting the effectiveness are encountered when using CTs alone. Hence, combined approaches are required to increase the efficacy. Chemo-photothermal therapy (CPT), which refers to the combined use of CTs and hyperthermia, can be a promising alternative to nanocarrier-mediated cancer therapy (1). CPT damages malignant cells by using heat converted from light by an agent and kills or slows the cell growth by cytotoxic CTs. Herein, paclitaxel-loaded nanocarriers (PCX-NP) were prepared and gold nanoparticles (AuNPs) were simultaneously synthesized to provide photothermal activity.

Materials and Methods: AuNPs-functionalized PCX-loaded nanocarriers (AU-PCX-NP) were prepared using a two-step method. First, nanoprecipitation method with a water-acetone system was adopted to develop PCX-NPs by using polylactic acid. Then, they were functionalized with AuNPs using the in-situ generation method. For comparison, blank nanocarriers (BLANK-NP), PCX-loaded nanocarriers (PCX-NP), and AuNPs-functionalized PCX-loaded nanocarriers (AU-PCX-NP) were fabricated. DLS analysis, morphologic evaluation, drug encapsulation and release studies were performed. Cell culture studies were carried out on MCF-7 and MDAMB231 human breast cancer cells.

Results: Particle sizes of all nanocarriers were less than 100 nm with a narrow size distribution and negative ζ-potential. Cryo-TEM images confirmed the in-situ generation of AuNPs in the nanocarriers. A dose-dependent increase in antiproliferative effect was observed after AU-PCX-NP exposure of the MDA-MB-231 with a significant difference compared to pure PCX.

Conclusions: We propose that nanotechnology-based combinational CPT appears as an alternative and more effective approach in comparison to mono-chemotherapy.

Acknowledgements: This study was supported by a grant of Ankara University Scientific Research Projects Coordination Office (18H0237003).

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OP023
DEVELOPMENT AND CHARACTERIZATION OF LENALIDOMIDE LOADED LIPOSOME AND NANOCOCHLEATE FOR THE TREATMENT OF BREAST CANCER

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Introduction: Liposomes are spherical lipid vesicles, usually 50-500 nm in size, consisting of one or more lipid bilayers. Since they consist of phospholipids, which are the building blocks of the body, they are biocompatible and non-toxic vesicular drug carrier systems (1). Nanocochleates are lipid-based, non-vesicular, stable, cylindrical, solid lipid bilayer-bearing systems obtained by precipitating a negatively charged lipid and a cation structure such as calcium. They are composed of phosphatidylserine, cholesterol and calcium (2). It was aimed to produce liposome and nanocochleate containing lenalidomide, an anticancer drug used in the treatment of cancers such as multiple myeloma and non-hodgkin lymphoma (3), to carry out characterization studies and to determine their cytotoxicity on the MDA breast cancer cell line.

Materials and Methods: Lenalidomid was gifted from Deva. Liposome was produced using 1,2-Dioleoyl-sn-glycero-3-phosphoethanolamine (DOPE) by the thin layer hydration method. Nanocochleate was obtained by precipitating dioleoylphosphatidylserine (DOPS), an anionic lipid, with the help of Ca+2 ions by adding CaCl2 (4). Formulations were characterized considering encapsulation efficiency, drug release, particle size, polydispersity index, zeta potential, scanning electron microscopy (SEM) images and cytotoxicity. In vitro release studies performed by static method in distilled water for 48 hours. The cytotoxicity of different concentrations of lenalidomide (7.5-1000 µg/mL), and liposome and nanocochleat containing dose of lenalidomide with anticancer effect (1000 µg/mL) were determined using the 3-(4,5-dimethyldiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay on the MDA cell line at 24 and 48 hours.

Results: It was observed from the SEM images that the liposomes were spherical and the nanocochleates were cylindrical. Particle sizes of the liposome and nanocochleat were 454.8±14.2 nm and 586.7±15.7 nm, and the zeta potentials were -21.2±1.7 mV and -38.9±3.9 mV, respectively. They had favorable encapsulation efficiency (77.3-83.4%). Drug release profiles were similar in both formulations with high burst effect up to 6 hours (87.3% for the liposome, 84.8% for the nanocochleate) and prolonged release up to 48 hours. According to MTT test results, lenalidomide-loaded liposomes caused higher cytotoxicity (lower viability/34%) at 24 hours, while lenalidomide-loaded nanocochleate allowed lower cytotoxicity (higher viability/41%). However, the nanocochleate showed higher cytotoxicity (28.9% viability) than the liposome (30.8% viability) at 48 hours

Conclusions: In conclusion, stable, nanosized lenalidomide-loaded liposome and nanocochleate with desired and superior morphology, encapsulation efficiency, particle size, zeta potential, in vitro release and cytotoxicity properties have been successfully developed. While both the formulations provided anticancer effects for up to 48 hours, it was concluded that nanocochleate may be more suitable than liposome for long-term anticancer effects

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OP024
METABOLOMIC AND LIPIDOMIC PROFILING OF SERUM USING MULTIPLATFORM MASS SPECTROMETRIC APPROACH

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Introduction: Metabolomics and lipidomics represent powerful and complementary tools for studying metabolism and its regulation. As metabolome and lipidome components exhibit different physicochemical properties, two distinct procedures are typically employed for their extraction before mass spectrometric analysis. However, in cases of limited sample availability, sequential extraction becomes necessary. The aim of this study was to establish an analytical workflow for metabolomic and lipidomic profiling of serum using a single extraction procedure, followed by multiplatform mass spectrometric analysis, to investigate the role of polymeric immunoglobulin receptor (pIgR) in a mouse model of obesity-induced insulin resistance.

Materials and Methods: Serum samples from pIgR–/– and pIgR+/+ mice on high-fat diet were processed by MTBE extraction. The polar fraction was analyzed by GC-TOF-MS after two-step derivatization. A shotgun lipidomics platform with direct infusion was used to analyze the hydrophobic fraction3. Analytical variability was monitored by quality assurance protocols, and statistical analysis was used to reveal significant alterations.

Results: Sample preparation, mass spectrometric analysis, data processing, and data analysis procedures were established to characterize the serum metabolome of pIgR knockout mice. We identified 158 small molecules by GC-MS among 743 features and quantified more than 250 lipid species encompassing 18 lipid classes by shotgun lipidomics. The analysis revealed altered levels of some organic acids, along with various phospholipid and lysophospholipids species.

Conclusions: The analytical workflow for sequential lipidomic and metabolomic profiling of serum was established to characterize pIgR–/– mice on HFD. The coverage was proven to be well-suited to characterize serum, revealing several changes in metabolites and lipid levels. Identified alterations may contribute to a better understanding of pIgR's role in the interplay between obesity, insulin resistance, and immunity.

Acknowledgements: ZCE gratefully acknowledges TUBITAK for her 2219 Fellowship.

OP025
A KINETIC STUDY ON THE DEGRADATION OF CIPROFLOXACIN USING UV KINETIC SPECTROPHOTOMETRIC MEASUREMENTS

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Introduction: The stability of pharmaceuticals is one of the very important indicators in drug research and development studies or preparations of drug formulations. In drug stability studies, degradation kinetics and reaction mechanisms for active ingredients in commercial products requires the estimation of the degradation rate under hydrolytic, oxidative, photolytic, and thermolytic stress conditions (1-2). In this study, the degradation kinetics and reaction mechanism of ciprofloxacin with sodium hypochlorite (NaOCl) were investigated. The rate constant and reaction order with an integrated rate equation were determined using UV kinetic spectrophotometric measurements. Ciprofloxacin is second generation fluoroquinolone group drugs that are effective against a wide range of bacterial infections such as respiratory and urinary tract infections (3).

Materials and Methods: Kinetic degradation reaction of ciprofloxacin at three different concentration levels (2.75, 5.50 and 8.25 µM) with NaOCl at pH 4 was studied. The UV spectra for the reaction of ciprofloxacin and NaOCl were recorded in the wavelength of 200-550 nm (0.2 nm increments) and in the time interval of 0.0-25.0 min (5 min increments).

Results: The above mentioned experimental conditions, the change in the absorption bands of ciprofloxacin at three different concentration level with NaOCl at pH 4 was observed. Decreases in ciprofloxacin concentration were plotted over time for calculating kinetic parameters.

Conclusions: The rate constant and reaction order were determined using an integrated rate equation. The order of the degradation reaction was determined and found as a second-order reaction. The rate constant for the degradation reaction of ciprofloxacin was found to be 1.94x10+4 M-1s-1. The results of this study are important because they can be used to determine the shelf life of the active ingredient in ciprofloxacin preparations.

Acknowledgements: This study was supported by Ankara University Scientific Research Fund (Project No. 10A3336001)

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OP026
LIPIDOMICS PROFILING USING DUAL STATIONARY PHASE COLUMNS

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Introduction: Detailed knowledge of "omics" approaches holds immense potential for understanding the mechanism of diseases, for their early diagnostics, choosing the personalized therapeutic strategy, and assessing its effectiveness (1). Recently, lipidomics, a comprehensive study of the pathways and networks of cellular lipids in biological systems, has become increasingly common in the general scientific community with the involvement of many researchers in diagnosing diseases. To understand the physiology of a biological system is only possible to analyze all metabolites and lipids in living organisms. However, analysis of metabolites that show significant physical and chemical differences cannot be carried out with a single method (1). The highest number of metabolites should be analyzed in a short period, considering time and analysis costs. Within the scope of our study, chiral and achiral stationary phase compounds containing two-module column systems were developed, and lipidomics analysis was performed.

Materials and Methods: Lipid analyses were carried out with LC-qTOF-MS in positive and negative ionization modes using a binary stationary phase system in which C18 and cellulose-based chiral stationary phases were packed in segmented columns.

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Results: In the study, 5 different columns were prepared by segmental packing. The ratios of C18 to cellulose material and the sequence of the stationary phases were tested in 8 stationary phase conditions. The number of lipids obtained from the two-module stationary-phase chromatographic system was more than that obtained from the single stationary-phase system. In addition, the ratio of cellulose to C18 and order in the chromatographic system also affected the results. It was found that the 7.5 cm chiral (10% Cellulose-3,5dichlorophenil-carbamate covalently attached to CS-36-300) and 2.5 cm C18 (3 x 100 mm) columns were superior for lipidomics analysis according to the other stationary phase ratios and sequences.

Conclusions: The higher number of lipid annotations may not only be due to chirality but also the simultaneous usage of a second separation mechanism may have separated lipids with similar physicochemical characteristics better than a single stationary phase. The developed method was applied to cancer cell lines for lipidomics evaluation.

Acknowledgments: This project (ID: 120Z600) was funded by The Scientific and Technological Research Council of Turkey (TÜBİTAK).

OP027

OPTIMIZATION BY BOX–BEHNKEN DESIGN OF FLIBANSERIN IN SUPPLEMENTS FOR WOMEN SEXUAL DESIRE ENHANCEMENT IN TÜRKIYE MARKETS USING HPLC AND THE GREENNESS ASSESSMENT OF THE DEVELOPED METHOD

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Introduction: Female sexual dysfunction is patient-specific and can manifest as changes in the patient's orgasm, vaginal pain, arousal problems, low desire, or hypoactive sexual desire disorder (HSDD) (1). Flibanserin (FLB) was the first drug approved by FDA as a medical treatment for HSDD in pre-menopausal women (2). The aim of this study was to develop a validated HPLC method with high accuracy and reliability for routine analysis of FLB.

Materials and Methods: The chromatographic method was developed using the Box-Behnken DoE method. During HPLC analyses, the moving phase flow rate sent to the system was 0.8 mL/min, the column temperature was selected as 38 °C, and the injection volume was determined as 10 µL. The water-acetonitrile mixture used as the mobile phase solution was used at a ratio of 45:55 (v/v %). Analyses were performed using a C18 column (100×4.6 mm i.d., 2.6µm). The highest absorbance of FLB was detected at 254 nm. Efavirenz was used as an internal standard.

Results: The method was fully validated according to ICH Q2 (R1) guideline. During the validation studies, the parameters of linearity, accuracy, precision, LOD and LOQ, robustness were investigated, and all results were found to be within the ranges in accordance with the standards. To determine the linearity of the developed method, FLB standard solutions were run for the PDA detector over a concentration range of 0.25–10 µg/mL, and the regression coefficient was higher than 0.99. LOD was 12.5 ng/mL, and the LOQ was 50 ng/mL.

Conclusions: In summary, analytical method validation was successfully performed by HPLC. With the developed method, various products sold in the market for sexual desire enhancer use were purchased and sample analysis was carried out under optimized conditions. The validated method was used for quantification and greenness assessment according to NEMI, GAPI, AGREE, and Analytical-Eco Scale.

Acknowledgements: This study was supported by a grant of Anadolu University Scientific research Projects Commission (Project No: 2005S039).

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OP028
ELECTROCHEMICAL DETERMINATION OF 2,6-DIISOPROPYLPHENOL ON AN EDGE PLANE PYROLYTIC GRAPHITE ELECTRODE

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Introduction: 2,6-diisopropylphenol (propofol), is a powerful intravenous hypnotic drug commonly utilized for maintaining anesthesia, as well as for sedation in intensive care settings (1). Edge plane pyrolytic graphite (EPPG) electrodes are beneficial for serving as electrode bases in electroanalysis because of their highly reactive edge plane locations (2). The purpose of this paper is to understand the electrochemical behaviour of propofol and develop a simple, sensitive, and fast method via differential pulse adsorptive stripping voltammetry (DPAdSV) technique.

Materials and Methods: Electrochemical experiments were conducted using an AUTOLAB-PGSTAT 30 electrochemical analysis system. An electrochemical cell was utilized, comprising an EPPG working electrode (3.0 mm diameter), a platinum wire counter electrode, and an Ag/AgCl (3 M NaCl) reference electrode. Propofol was provided from DEVA holding A.S., and stock solutions of 356.56 ppm prepared in ethanol and stored at +4 °C.

Results: The influence of pH and various supporting electrolytes on the electrochemical behaviour of 106.97 ppm propofol containing constant 20% ethanol was investigated in the pH range from 1.00 to 12.00 using cyclic voltammetry (CV), as well as differential pulse (DP), and square wave (SW) voltammetry techniques on EPPG electrode. The pH 4.68 acetate buffer was selected for the further studies. The scan rate studies in the ranged from 0.01 to 0.5 Vs–1, applied to a solution containing 106.97 ppm propofol by CV. Results of scan rate studies revealed that the electrochemical reactions occur through mixed diffusion-adsorption controlled process.

DPV were optimized as a step potential of 5 mV, an amplitude of 200 mV, a modulation time of 25 mV, and an interval time of 200 mV for a solution containing 17.93 ppm of propofol. Optimal stripping conditions for DPV were defined to be a deposition potential of 0 V and a deposition time of 120 s. Under these optimized conditions, a linear range from 0.36 to 1.79 ppm with a detection limit of 0.04 ppm was achieved. The developed method was applied to the pharmaceutical dosage forms. % Recovery values was found to be 100.16 with the % relative standard deviation of 5.77. The effect of possible interferents such as K+, Cl–, Na+, Ca2+, NO3–, glucose, ascorbic acid, and dopamine on the electrochemical determination of propofol was investigated.

Conclusions: A simple, sensitive, rapid, and technique was developed in acetate buffer (pH 4.68) for the quantification of propofol in pharmaceutical dosage forms.

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OP029
MOLECULARLY IMPRINTED ELECTROCHEMICAL SENSOR FOR THE ULTRA-SENSITIVE AND SELECTIVE DETECTION OF NADIFLOXACIN

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Introduction: Nadifloxacin (NAD) is a topical antibiotic that is a second generation fluoroquinolone with broad-spectrum antibacterial activity. It is used to treat acne, an inflammatory skin disease seen in young adults and adolescents [1, 2]. This study aims to develop a new highly sensitive, simple, rapid and inexpensive method for the determination of NAD in commercial serum samples.

Materials and Methods: A new molecularly imprinted polymer (MIP) film was synthesized on a glassy carbon electrode (GCE) by electorpolymerization method using 4-amino benzoic acid (4-ABA) as a functional monomer and nadifloxacin (NAD) as a template molecule. Optimization of the MIP film was carried out using [Fe(CN)6]3/4- as a redox probe. The removal and rebinding of the template molecule were investigated by differential pulse voltammetry (DPV) and electrochemical impedance spectroscopy (EIS) methods.

Results: The limit of detection (LOD) and limit of determination (LOQ) of the NAD on EP-4ABA@MIP/GCE were determined as 0.12 pM and 0.39 pM, respectively, and the linearity range was found between 1.0 pM and 10 pM.

Conclusions: The electrochemical MIP sensor EP-4ABA@MIP/GCE was developed to determine NAD with remarkable sensitivity and a very low detection limit, surpassing the capabilities of most analytical methods used in pharmaceutical analysis.

Acknowledgements: Thanks the financial support from the Scientific and Technological Research Council of Türkiye (TUBITAK) under the BIDEB/2218 National Postdoctoral Research Scholarship Program.

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OP030
ELECTROCHEMICAL DISCRIMINATION OF AN INFECTIOUS BACTERİUM FROM OTHER BACTERİAL SPECIES USING MOLECULARLY IMPRINTED POLYMERS

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Introduction: Electrochemical biosensors, which adeptly convert biological responses into quantifiable electrical signals, have gained substantial prominence in recent years. They are extensively employed for the precise detection of a diverse array of analytes, including proteins, pathogens, and more (1). Molecularly imprinted polymers (MIPs) are synthetic materials that have specific cavities designed to recognize and bind selectively to a target molecule. MIPs enable sensitive determination by facilitating binding similar to the antigen-antibody interaction with the target molecule. Enterococcus faecium, which is highly resistant to antibiotics, causes many nosocomial infections and is detected using conventional methods such as culture-based techniques and PCR. These methods are time-consuming and expensive (2). In our study, we aim to develop an MIP-based electrochemical biosensor for detecting E. faecium. from a bacteria mixture in both an artificial and real urine samples.

Materials and Methods: E. faecium-imprinted polypyrrole structure was formed through electropolymerization in buffer solution containing E. faecium and pyrrole monomer using Cyclic Voltammetry (CV). The bacteria coated on the polymer surface were removed by treatment with a removal agent to provide the MIP structure. Finally, MIP-modified electrodes were re-treated with E. faecium and other bacteria such as E. faecalis, and Electrochemical Impedance Spectroscopy (EIS) measurements were conducted in K3/4[Fe(CN)6] solution.

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Results: As a result of the polypyrrole coating on the surface, both conductivity and electroactive surface area have increased. After the MIP structure was formed, treatment with increasing concentrations of E. faecium resulted in an increase in charge transfer resistance (Rct) values. For E. faecium samples prepared in both artificial and real urine, treatment these samples with MIP-modified electrodes also results in a significant increase in Rct values. The response of the developed biosensor to other urinary tract infection-causing bacteria, particularly E. faecalis, is significantly lower compared to the E. faecium.

Conclusions: The limit of detection (LOD) was found below 10 CFU/mL. This value indicates the sensitive detection was achieved compared to conventional methods. The low responses given to structurally similar E. faecalis and other bacteria demonstrate high selectivity of the developed biosensor. Given its low LOD and high selectivity in detecting substances in urine samples, the developed biosensor could indeed serve as an alternative to conventional methods

Acknowledgements: This study was supported by the grant of Izmir Katip Celebi University Scientific Research Projects Coordination Unit (Project No: 2022-GAP-ECZF-0009).

OP031
INVESTIGATING THE INTERACTION OF AN ANTICANCER DRUG PALBOCICLIB WITH HUMAN SERUM ALBUMIN USING SPECTROSCOPIC AND ELECTROCHEMICAL METHODS

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Introduction: Palbociclib (PAL) is a pharmaceutical compound specifically designed to combat HR-positive and HER2-negative breast cancer(Alghamdi et al., 2020). Additionally, it functions as a specific inhibitor of Cyclin-dependent kinases CDK4 and CDK6. Palbociclib is the initial cyclin-dependent kinase 4/6 (CDK4/6) inhibitor that has been authorized for use in cancer therapy. The drug' features for binding to protein in vivo also have a big impact on its medicinal properties(Zahirul Kabir et al., 2023). In this study, we aimed to characterize the biomolecular association between PAL and albumin from human serum (HSA), the major transporter in the blood plasma using fluorescence, UV-Vis absorption and voltammetric techniques.

Materials and Methods: Monitoring fluorescence signals on an Agilent Cary Eclipse spectrofluorometer with a Xenon light determined PAL–HSA titrations. A constant protein concentration of 3 µM was titrated with increasing concentrations (2–12 µM with 2 µM intervals) using PAL in tubes, with PBS adding 3 mL total volume. Before 60 mins of incubation at 288, 298 and 307 K, the solution mixtures were properly vortexed. After placing the sample-loaded cuvette in a Peltier temperature-regulating cell holder, it was incubated for 6 mins at the chosen temperatures. HSA fluorescence signals (λex = 280 nm and λem = 300-450 nm) were measured with and without progressing PAL concentrations.

Results: PAL-induced HSA fluorescence intensity changes suggested PAL-HSA complex formation. The Stern-Volmer quenching constants and emission spectrum findings showed static quenching of HSA fluorescence. PAL and HSA have an intermediate binding affinity (105), according to quenching data. The PAL–HSA complex's main contact forces were hydrophobic and hydrogen bonds, according to thermodynamic data. The voltammetric and molecular docking analysis confirmed PAL–HSA complex formation. The preferred PAL binding location in HSA was found using competitive site-markers displacement.

Conclusions: The changes in the emission spectra and the decrease in KSV values with increasing temperature suggest that the fluorescence quenching of HSA caused by PAL remains static. The pharmacokinetics and subsequent development of the drug will benefit from the above findings.

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OP032
DEVELOPMENT OF CUMIN ESSENTIAL OIL NANOEMULGEL FORMULATIONS FOR THE TREATMENT OF VAGINAL CANDIDIASIS: IN VITRO ANTIFUNGAL ACTIVITY AND CYTOTOXICITY STUDIES

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Introduction: Vaginal candidiasis (VC), is a prevalent mucosal infection caused by various Candida species (1). It is a global health concern due to its widespread occurrence, ability to form biofilms, and the emergence of drug resistance. Around 75% of women experience an episode of candida vaginitis at least once in their lifetime, making it one of the most common reasons for women to seek healthcare (2). VC presents with symptoms such as pain, itching, soreness, redness, and swelling of the vulva which significantly affects patients' quality of life (1). Several studies have shown that cumin seeds essential oil is an effective remedy for VC due to its bioactive molecules such as γ-terpinene, p-cymene and β-pinene (3,4). Conventional vaginal formulations like creams, gels, suppositories, and ointments have limitations in terms of deposition on the vaginal surface and penetrating to deeper layers of the tissue due to the self-cleaning nature of the vagina (5). Hence, the objective of this study is to develop a nanoemulgel formulation that improves the therapeutic efficacy of cumin essential oil by enhancing its bioadhesivity, decreasing toxicity and ensuring ease of application for patients.

Materials and Methods: Cumin oil (Orlife Global, Türkiye), Tween20 (Sigma, Germany), water (distilled) and Capryol90 (obtained as a gift sample from Gattefossé, France) were used in the nanoemulsion optimization study. Optimization involved parameters like total oil/surfactant ratio, essential oil/total oil ratio, and total water content using Minitab(R) 3X3 Taguchi Orthogonal Design. Formulated nanoemulsions were characterized in terms of organoleptic properties, viscosity, droplet size, zeta potential and pH values. Selected formulation was incorporated into bioadhesive gel bases (sodium alginate or carboxymethyl cellulose) and further characterized in terms of spreadability, viscosity and ex-vivo mucoadhesion properties. Antifungal activities against Candida species, in-vitro cytotoxicity and stability were also evaluated.

Results: Selected optimum formulation has a droplet size of 11.68, polydispersity index of 0.24, zeta potential of -3.05 mV and pH value of 3.9, which is suitable for vaginal application. Both nanoemulsion and nanoemulgels were effective against Candida species and were not cytotoxic on Vero cells. Moreover, nanoemulgel formulation displayed good ex-vivo mucoadhesive properties and spreadability features and all of the formulations were stable after a 1 month storage period.

Conclusions: This study demonstrated that the optimized cumin essential oil nanoemulgel formulations exhibit high potential for vaginal candidiasis treatment due to their good antifungal activity, mucoadhesion, low toxicity and easy application.

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OP033
DEVELOPMENT AND IN VITRO EVALUATION OF INDOMETHACIN-LOADED NANOPARTICLES.

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Introduction: Indomethacin is a non-steroidal anti-inflammatory drug that has various side effects and low solubility in water (1). Nanoparticles are defined as particulate dispersions or solid particles in the size of 10-1000 nanometers, which the drug is dissolved, entrapped or encapsulated to a matrix (2). Therefore, this study aims at overcoming those challenges by loading the drug into SLNs and PNPs.

Materials and Methods: Indomethacin (IND) (kindly gifted by Deva, Turkiye), Dynasan® 116 (Condea Chemie GmbH, Germany), Eudragit® RLPO (Röhm GmbH, Germany), Eudragit® RSPO (Röhm GmbH, Germany). All other chemicals were in analytical grade. For optimum lipid for the SLN formulation, 5 different lipids were tested for attached IND molecules by preparing formulations without surfactants. SLN formulation was prepared by using emulsifying method and PNP formulation was made by using emulsifying – solvent evaporation method. HPLC method was used for determination of Indomethacin. Prepared formulations were evaluated for particle size (PS), polydispersity index (PDI), zeta potential (ZP) and encapsulation efficiency (%EE).

Results: Formulations prepared without using surfactants showed that the formulation with Dynasan® 116 had the most amount of IND loaded.

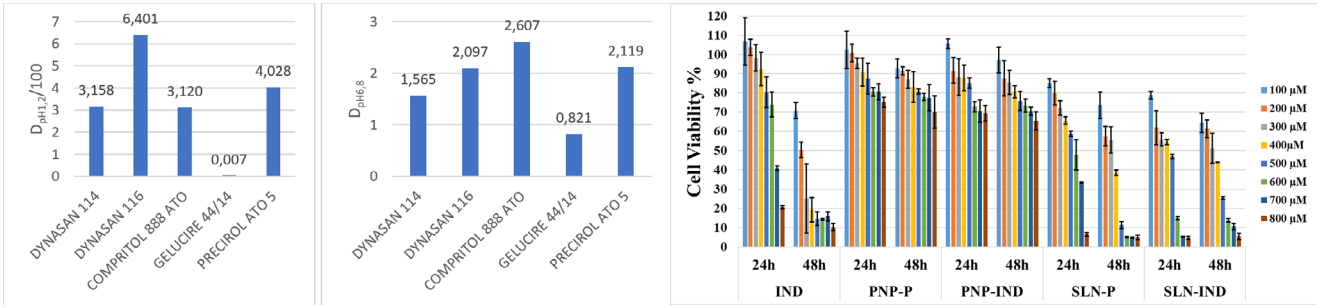

Figure 1. Calculated amount of IND in different lipids and MTT assay results.

Table 1. Characterizations of IND-loaded SLN and PNP formulations (n=3)

Code	PS (nm)	PDI	ZP (mV)	%EE
SLN	74,66	0,368	-18,4	3,8 ± 0,17
PNP	181,9	0,452	-18,8	32,6 ± 0,04

Conclusions: Dynasan® 116 was determined as the optimum lipid for the SLN formulation according to the results of IND amount loaded. IND-loaded SLN and PNP formulations' zeta potential and particle size results indicated that formulations have good stability (3). Encapsulation efficiency values are appropriate as desired. Further studies such as *in vitro* dissolution and drug releasing tests can be considered. As a result of MTT analysis of indomethacin application for 24 and 48 hours, a linear correlation was observed between drug concentration and cell viability, and it was determined that the PNP formulation had less toxic effects among the formulations. This proves that the PNP nanocarrier is safer for normal cells.

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OP034
DEVELOPMENT AND CHARACTERIZATION OF LACOSAMIDE-LOADED THERMOSENSITIVE IN SITU GELS FOR PROLONGED OCULAR RESIDENCE TIME

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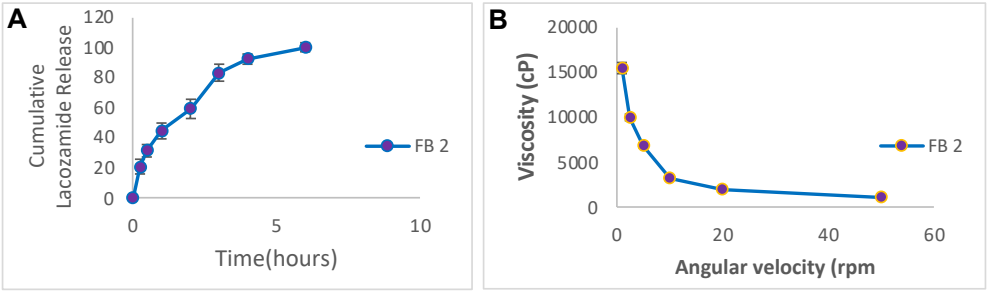
Introduction: Due to its resemblance to dry eye disease symptoms, corneal neuropathic pain has posed a significant challenge for ophthalmologists. Despite its similarities, conventional dry eye treatments have proven ineffective (1). Therefore, there has been growing interest in targeting cold thermoreceptors as a potential therapeutic approach. It has been demonstrated that topical lacosamide reduces the hyperexcitability of cold-sensitive corneal nerve terminals (2). The aim of this study is to develop lacosamide-loaded thermosensitive in situ gels and to prolong the ocular residence time of lacosamide, thereby reducing the need for frequent dosing.

Materials and Methods: During the formulation of thermosensitive gels, poloxamer 407 and 188 are incorporated to induce gelation with heat, and hydroxypropyl methyl cellulose is used to enhance viscosity. The pH, clarity, gelation temperature and viscosity of the in situ gels were assessed, leading to the selection of a specific formulation (FB 2) (Table 1). Subsequently, lacosamide was loaded into FB 2, and release and rheological studies performed and MTT analyses were conducted using ARPE-19 and L929 cell lines.

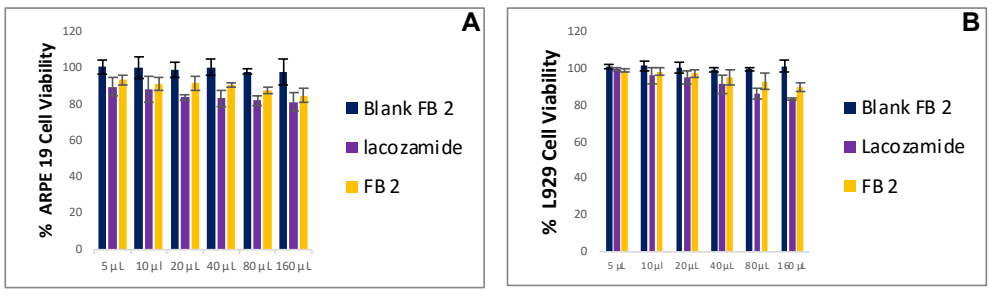
Formulation Code	HPMC (4k) (%)	Poloxamer 188(%)	Poloxamer 407 (%)	Viscosity (25°C) (Cp)	Viscosity (35°C) (Cp)	pH	Gelation temp (°C)	Clearty
FB 1	0,5	3	12	502±47	6874±174	7,15±0,01	33±0,41	Clear
FB 2	1	3	12	498±54	7012±145	7,09±0,03	34±0,52	Clear
FB 3	0,5	3	15	606±74	7913±165	7,11±0,01	31±0,34	Clear
FB 4	1	3	15	627±51	8412±207	7,07±0,02	30±0,43	Clear
FB 5	0,5	3	18	874±92	9011±278	7,1±0,01	28±0,29	Clear
FB 6	1	3	18	901±65	9577±302	7,04±0,05	27±0,34	Clear

Results: As a result of the release studies, it was determined that FB 2 made a 60% burst release at the end of the 2nd hour, and then made a controlled release until the end of the 6th hour. FB 2 at their gelling temperatures demonstrated pseudoplastic flow (shear thinning system) similar to tear fluid when the rheological behaviors were analyzed (Figure 1 a-1b).



In studies conducted on both ARPE-19 and L929 cell lines, a decrease in cell viability was observed with increasing doses; however, it was noted that cell viability remained above 85% even at the highest dose applied (Figure 2 a-2b).

Conclusions: As a result, the in situ gel was successfully produced and characterized, demonstrating a release duration of six hours. Furthermore, it was determined to be non-toxic in two different cell studies.



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OP035
PAROXETINE-LOADED NANOPARTICLES: DEVOLOPMENT AND CHARACTERIZATION USING BOX-BEHNKEN DESIGN

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Introduction: The prevalence of depression in cancer patients is almost three times higher than that of the non-cancerous population. In addition to chemotherapy, depression treatment including selective serotonin reuptake inhibitors group antidepressants is widely used in patients treated in oncology units. Recent pre-clinical studies suggest that paroxetine, an SSRI, inhibits the growth of cancer cells, induces apoptosis and shows synergistic effect when used in combination with traditional chemotherapeutic drugs (1).

Materials and Methods: In this study, paroxetine-loaded polycaprolactone (PCL) nanoparticle formulations were prepared by double emulsion-solvent evaporation method (2) and optimized by Box-Behnken Design (BBD) (3). In the scope of the 33 BBD; nineteen different formulations were prepared by using the drug-polymer ratio, sonication power and oil phase volume as independent variables, whereas choosing the particle size, particle size distribution, encapsulation efficiency and the cumulative drug released % at the end of the 12th hour as dependent variables.

Results: It was observed that the particle size of the formulations prepared using the BBD was between 243-468 nm and the particle size distribution was between 0.072-0.0597. While the encapsulation efficiency of paroxetine was observed to be between 71-90%, the amount of the drug released from the nanoparticles at the end of the 12th hour was obtained to be between 22-100%.

Conclusions: In this study, PCL nanoparticles containing paroxetine were successfully prepared as a new candidate drug delivery system for colorectal cancer treatment. By employing the experimental design approach, paroxetine-loaded nanoparticulate formulations with targeted physicochemical properties could be developed by performing relatively fewer experiments.

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OP036
POTENTIAL ASSOCIATIONS BETWEEN SEVERAL GENE POLYMORPHISMS AND SJOGREN'S SYNDROME

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Introduction: Sjögren's syndrome is a chronic autoimmune disorder of unspecified etiology implicating exocrine glands. SS patients illustrate dry eyes and mouth, joint pain, fever and neurological symptoms. Hormones, immune dysregulation, and environmental and genetic factors play the primary roles in the development of the disease. Previous studies reported that HLA-II, STAT4, BAFF and TINIP1 polymorphisms have a pivotal role in SS development, however, the variant on each gene has not been investigated in the Turkish population. Therefore, this study aims to identify and evaluate the association between four variants of the four mentioned genes above and the development of Sjögren's syndrome.

Materials and Methods: This study recruited 40 healthy subjects and 115 patients with Sjögren's syndrome in a Turkish population. All genomic variants were detected using the PCR-RFLP technique. We observed that SNP rs1130380, rs7574865, rs9514828, and rs17728338 were associated with SS development. We herein highlighted that the subjects with 1/2 or 2/2 Allele (%) had a higher susceptibility to SS development than those with the 1/1 Allele. Furthermore, the allele frequency of each variant was then assessed in multiple continents, including African, American, European, and Asian cohorts.

Results: Interestingly, our data shows that upregulating variants are at higher frequencies compared to European American and Asian populations, which implies that Turkish populations might be relatively susceptible to SS development related to these variants.

Conclusions: The results indicated that all variants were significantly associated with the development of the SS disease in the Turkish population.

OP037
EFFECTS OF QUERCETIN AND VITAMIN E AGAINST CYPERMETHRIN-INDUCED TOXICITY IN LUNG CELLS

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Introduction: Cypermethrin is a type II synthetic pyrethroid pesticide widely used in agriculture and consumer applications (1). It has been reported that cypermethrin has toxic effects on various tissues and organs (2). Pyrethroids can contaminate air, soil and water and enter the body through various routes, causing toxic effects on the lungs (3,4). The present study aimed to investigate the protective effects of quercetin and vitamin E on cypermethrin-induced toxicity in the A549 human lung cell line.

Materials and Methods: Cytotoxic effect of cypermethrin was evaluated in the human lung cell line (A549) by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) test. In addition, the possible protective effects of quercetin and vitamin E against the toxicity caused by cypermethrin were investigated with the MTT test at two different time intervals (24 and 48 hours). Levels of intracellular reactive oxygen species (ROS) were determined using the oxidation-sensitive fluorescent probes 2,7-dichloro-fluorescent acetate (DCFH-DA) and changes in the mitochondrial membrane potential (MMP) were detected using JC-1 commercial kit. The concentrations used in the experiments were selected based on the IC50 values of cypermethrin.

Results: According to the MTT test, it was observed that quercetin and vitamin E increased cell viability at certain concentrations against cypermethrin toxicity after 24 and 48 hours of exposure, and the effects of vitamin E were found to be more significant. According to the DCFH-DA method, it was determined that cypermethrin increased ROS levels at certain concentrations and it was observed that the antioxidant effects of vitamin E were more significant than quercetin. Among the observed findings are that cypermethrin reduces the mitochondrial membrane potential at high concentrations and vitamin E has a significant protective effect.

Conclusions: The findings showed that quercetin may be slightly protective against possible cypermethrin toxicity, while vitamin E may be significantly protective. In addition, the results will help to elucidate the toxicity mechanism of cypermethrin in more detail with future studies.

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OP038
RESEARCH ON UNUSED AND WASTED DRUGS IN ANKARA PROVINCE

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Introduction: The issue of unused and wasted pharmaceuticals is becoming increasingly prevalent on a global scale. The health sector and the consumption of health-related products are expanding at a rapid pace, yet there is currently no established process for the recovery of waste pharmaceutical molecules. Consequently, on-site separation and waste minimisation methods are being implemented or attempted in Turkey and across the globe with the aim of reducing pharmaceutical waste.

Materials and Methods: The household waste drugs were collected at three different eco-social levels and recorded as drug features (ATC classification, dosage form, expiry date, amount of used and so forth). Additionally, past data was gathered for analysis. The results will be statistically compared by distribution in different features in order to make an analysis with the waste drugs produced by pharmacies.

Results: In 2020, approximately 1.5 tons of household waste drugs were collected per month in Ankara. Furthermore, when societal habits are examined, it is evident that waste/unused drugs are discarded and flushed away. Our preliminary findings indicate that cold and flu formulations (n:96), painkillers (n:78), and vitamin combinations (n:28) were found to be the most commonly wasted. The most prevalent dosage forms were tablets (44.86%), capsules (4.64%) and injectable forms (5.72%). The majority of collected drugs were expired (56.75%), with their original secondary container (46.25%). A further 10.75% of the drugs were never used. When the expired drugs were examined, it was found that they had been kept at home for approximately 8 months after their expiry date.

Conclusions: Waste management is a crucial process for all countries. Methods such as incineration and underground burial are employed for non-recyclable wastes, yet these practices have the potential to exacerbate environmental concerns. A review of studies conducted for the pharmacy and pharmaceutical industry revealed that waste pharmaceuticals are increasingly accumulating in Turkey, mirroring trends observed globally. This highlights the need for a more comprehensive understanding of the composition of waste pharmaceuticals to inform effective waste management strategies.

Acknowledgements: Our project will be carried out in partnership with Ankara Metropolitan Municipality and Ankara Chamber of Pharmacists

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OP039
A SURVEY STUDY MEASURING PRIMARY HEALTHCARE PROVIDERS' KNOWLEDGE OF ALZHEIMER'S DISEASE IN TURKEY

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Introduction: Alzheimer's disease (AD) is the leading cause of dementia in the elderly and requires intensive professional care (1). Our objective was to evaluate the knowledge of primary healthcare providers, specifically Family Physicians (FPs) and community pharmacists (CPs) regarding AD and its treatment.

Materials and Methods: A prospective, descriptive, observational study utilizing Google Forms sent by email or message to Istanbul FPs and CPs in June–July 2023. Turkish modified the Alzheimer's Disease Knowledge Scale (ADKS) and Alzheimer's Medicines Knowledge Level Questionnaire (AMKLQ) were utilized in this study.

Results: 63 FPs with a mean age of 35.3 ±7.8 and 138 CPs with a mean age of 38.6 ±12.6 enrolled to the study. There was no statistically significant difference between FPs and CPs in terms of total ADKS score (19.82±2.30 vs 19.23±3.08, p=0.136), but there was a significant difference in terms of total AMKLQ score (4.31±1.40 vs 3.81±1.49, p=0.020). Healthcare providers with Alzheimer's training had a higher total AMKLQ score (OR =1.08 CI 95% [1.03-1.14], p=0.012).

Conclusions: FP' knowledge of AD is on par with that of CPs. However, it has been noted that FPs are more proficient at providing precise answers to the AMKLQ and ADKS questions, which cover critical information about the management of AD. Professional education was shown to be the only factor in determining who had the highest mean AMKLQ score. When taken together, these points highlight the importance of primary healthcare providers receiving extensive, continuous education about AD and its treatment.

Acknowledgments: None.

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OP040
THE EVALUATION OF RISK FACTORS OF CANDIDEMIA OF LIVER TRANSPLANTATION RECIPIENTS.

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Introduction: Liver transplantation recipients frequently encounter multi-drug resistance, opportunistic and invasive fungal infections (IFI) (1). Candidiasis (60%-80%) is the most commonly observed IFI, followed by aspergillosis (1%-8%) (2). IFIs can lead to graft failure, increased morbidity, and mortality (3). Our aim was to determine the relationship between candidemia and the clinical features of liver transplantation recipients.

Materials and Methods: The study was conducted as a retrospective case control study and is ongoing so the preliminary results were shared. The sample size was calculated as at least 93 individuals using G-power program by taking α=0.05, power (1-β) =0.80 at a confidence level of 95% and case to control ratio as 1:2 (4). 108 patients, comprising 36 cases and 72 controls were included in the study. Groups were matched for length of hospital stay, age, and neutropenia status. Data were collected retrospectively by reviewing patients' medical records. Total parenteral nutrition (TPN) within the last week for at least two days before candidemia, concurrent positivity of Cytomegalovirus-Polymerase Chain Reaction (CMV-PCR) with candidemia, and mortality within 30 days after candidemia were evaluated. The study received approval from the university's ethics committee, and IBM SPSS 23.0 was used for statistical analysis.

Results: The mean age (years) was 53.11±9.94 for the case group, and 52.78±10.19 for the control group. The median length of hospital stay was 35.5 days (IQR: 24.7-47) for case group, and 40 days (IQR: 31-58.7) for control group. There was no statistically significant difference between the groups in terms of age and length of hospital stay. Mortality was higher in patients with candidemia (p=0.002). Total Parenteral Nutirition (TPN) and positive CMV-PCR were found to be associated with candidemia (p=0.04, p=0.015). Malignancy and chronic kidney disease were found to be related to candidemia (p=0.004, p=0.011). Candida albicans was the most seen species of candidemia (41.7%). There were no relationship between serum drug concentrations of immunosuppressive regimens and candidema.

Conclusions: Candida albicans was reported as the most seen isolate causing invasive candidemia, and mortality rate was higher in patients with candidemia, similar to our study. While the use of broad spectrum antibiotics, diabetes melllitus, TPN, hemodialysis were reported as risk factors for candidemia in the literature, our study found TPN, malignancy, positive CMV-PCR and chronic kidney disease to be associated with candidemia (5). Since the risk factors for candidemia vary, clinicians should pay attention to patient characteristics in liver transplant recipients.

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OP041
VITAMIN D AWARENESS AND PERCEPTIONS AMONG TURKISH PATIENTS

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Introduction: Vitamin D plays a crucial role in several essential physiological processes within the human body (1). The insufficiency of this vitamins a significant global public health concern and is linked to a wide range of illnesses (2). The present study aimed to evaluate the knowledge, attitudes, and behaviors pertaining to vitamin D across the general population of Istanbul, Turkey.

Materials and Methods: A cross-sectional observational study was done to analyze the characteristics of clients who frequently visit pharmacies in Istanbul and seek for vitamin D supplements. The research data was collected during four months from February 2023 to June 2023 using a self-administered questionnaire. The questionnaire of 31 multiple-choice question (MCQ) items, categorized into socio-demographic characteristics and participants' attitudes and knowledge concerning vitamin D.

Results: The study entailed the recruitment of a sample size of 129 individuals, of which approximately 65.11% were female. Although 98.4% of the participants have heard before about vitamin D , only 10.9% showed the ability to identify sunlight as the primary sources of vitamin D. While 62.8% of the participants demonstrated awareness of the symptoms associated with vitamin D deficiency, only 55.9% of the clients received information about vitamin D and its deficiency from a healthcare provider. Out of the participants, 45.7% are exposed to the sun, whereas only 20.9% of the study group stated using sunscreen. The characteristics that were shown to be connected with good knowledge were female gender ($P < 0.045$) and those who had completed high school ($P < 0.013$).

Conclusions: The findings of this study indicate a lack of adequate information and attitude among the clients regarding vitamin D and its deficiency. Hence, our research highlights the necessity of providing education and raising awareness among the community regarding vitamin D and the prevention of its deficiency.

Acknowledgments: None.

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OP042
MEPACRINE, A CANDIDATE FOR CSPG4 TARGETED TREATMENT IN CHORDOMA USING IN SILICO TECHNIQUE

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Introduction: Understanding how the immune system fights cancer has greatly influenced the development of immunotherapy to start taking place among the treatment protocols as a powerful tool in cancer treatment. Recently, increasing studies have focused on the molecular basis of immunotherapy and the development of combining strategies with classical treatment options(1). Chordoma is a rare type of bone cancer that occurs in the spine and skull base. It is frequently resistant to chemotherapy and radiotherapy(2). These emphasize the need for the development of innovative and focused treatment options such as immunotherapy to enhance chordoma patient outcomes(3). There is a growing interest in immunotherapy agents for chordomas. This study aimed to investigate immunotherapeutic agents targeting the Chondroitin Sulfate Proteoglycan 4 (CSPG4), expressed in chordoma tumors(4) using in silico tools.

Materials and Methods: In-silico screening by Gene2Drug, a Pathway-based Rational Drug Repositioning website was used to be able to find compounds that target CSPG4 Gene based on PRISM viability assays on 9 cell lines that are related to Chordoma and Chondrosarcoma.

Results: A total of 135 compounds were analyzed using DRUG Sensitivity (PRISM Repurposing Primary) and PRISM Repurposing Public 23Q2 Tool. Interestingly, a total of seven compounds including phenazopyridine, amitriptyline, zuclopenthixol, mepacrine, lasalocid, verapamil, and alexidine were significantly sensitive ($P < 1 E–2$). Yet, mepacrine showed the most promising potential as a CSPG4-targeted treatment candidate in chordoma.

Conclusions: This in-silico study showed a sensitivity of the CSPG4 gene in cancer cell lines to several compounds including mepacrine. Therefore, holding promises for mepacrine and CSPG4 targeted treatment strategies in chordoma. It is advised to further investigate the drug-mediated pathways using computational techniques.

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OP043
SECONDARY METABOLITES AND ACTIVITIES OF MARINE FUNGI FROM TURKEY AND ANTARCTICA

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Introduction: The marine environment is a rich source of natural bioactive compounds In recent years, many new bioactive compounds have been isolated from marine organisms (1). To date, approximately 31500 substances have been obtained from different marine sources nearly half of them show biological activity (2). Marine- fungi; produce a wide range of bioactive compounds such as antimicrobial, antiviral, cytotoxic and antioxidant active substances (3). The aim of this study is presenting the results of bioactivity studies and isolated secondary metabolites of marine fungi obtained from both Turkish seas and Antarctica.

Materials and Methods: Marine samples were collected from Turkish seas and regional seas around Antarctica. The disk diffusion technique was used to determined antimicrobial activity of isolated marine-derived fungi extracts. DPPH, SO, NO, and ABTS assays were used for antioxidant activity (4). MTT assay was used for testing cytotoxic activity.

Results: In total, 37 secondary metabolite was isolated from 7 fungal species New austin-type meroterpenes are among these isolated substances. The activities of both these fungi extracts and fungi extracts isolated from Antarctica were tested.

Conclusions: Marine sources are important for discovering new bioactive natural products.

Acknowledgements: This study was supported by a grant of TUBITAK (114S916).

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OP044
CHEMICAL COMPOSITION AND BIOACTIVE POTENTIAL OF SCORZONERA KETZKHOWELII SOSN. EX GROSSH.

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Introduction: Scorzonera L. (Asteraceae) genus is represented in Türkiye with 59 taxa, of which 31 are endemic (1). They are used in the treatment of cardiovascular diseases, kidney diseases, stomach pain, infertility and as an analgesic, wound healer, galactagog, and anthelmintic. Numerous activity and chemical structure elucidation studies have been carried out on Scorzonera species (2, 3). Scorzonera ketzkhowelii Sosn. ex Grossh. was reported as a new species in the Flora of Turkey in 2010 (4). The first study related to this species was published in 2024 and focuses on its antimicrobial effect and the chemical composition of its dichloromethane extract (5). In this study, it is aimed to investigate the in vitro anti-inflammatory, anti-cholinesterase, and anti-oxidant activities of extracts obtained from Scorzonera ketzkhowelii and additionally, the isolation and structure determination of phenolic compounds found in the ethyl acetate extract, as well as the elucidation of their structure and potential biological activities through in-silico molecular modeling.

Materials and Methods: Scorzonera ketzkhowelii specimens collected in Yusufeli/Artvin, Turkey, altitude 2122m. Voucher: ISTE 115803, Istanbul University's Faculty of Pharmacy Herbarium. Total phenolic compound and flavonoid contents and also anti-oxidant, anti-inflammatory, and anti-acetylcholinesterase activities were determined on sub-extracts (petroleum ether, dichloromethane, ethyl acetate, and n-butanol sub-extracts) prepared from ethanol extracts obtained by percolation method. Phenolic compounds, isolated from ethyl acetate sub-extracts exhibiting the highest antioxidant activity, underwent structural elucidation via column chromatography and spectroscopic methods. Subsequently, the biological activities of isolated pure compounds were assessed using molecular modeling methods.

Results: The ethyl acetate extracts from both aerial and subaerial parts emerged as potent sources of phenolic compounds and flavonoids, exhibiting remarkable antioxidant activity. All fractions exhibited potent inhibition against COX-I and COX-II enzymes, with notable inhibitory effects observed in the ethyl acetate and dichloromethane sub-extracts against AChE.

Twelve phenolic compounds were isolated and characterized from the ethyl acetate sub-extracts, including hydrangenol (1), 4-hydroxy benzaldehyde (2), luteolin (3), esculin (4), 3-O-caffeoylquinic acid ethyl ester (5), 3-O-caffeoylquinic acid methyl ester (6), kaempferol 3-O-β-glucopyranoside (7), quercetin 3-O-α-arabinopyranoside (8), 3,5-di-O-caffeoylquinic acid ethyl ester (9), thunberginol F 7-O-β-D-glucopyranoside (10), hydrangeic acid 4'-O-β-D-glucopyranoside (11), and 3-O-caffeoylquinic acid (12). Additionally, the inhibitory effects of these compounds were assessed against TNFα, COX-I, COX-II, human Cyp-P450, and hAChE, through molecular docking studies. According to the molecular docking and dynamics studies, compound 9 emerged as particularly noteworthy across all complexes, exhibiting stable binding modes and promising interactions with key residues involved in inhibition.

Conclusions: Overall, our study contributes to the understanding of the therapeutic potential of Scorzonera ketzkhowelii and highlights the importance of further exploration into its bioactive compounds for the development of novel pharmaceuticals with anti-inflammatory, antioxidant, and anticholinesterase activities.

Acknowledgements: This work was supported by the Research Fund of Istanbul University under Project No. 34159

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OP045
EVALUATION OF AGRICULTURAL WASTE PARTS OF CUCURBITA SPECIES IN TERMS OF BIOLOGICAL ACTIVITY POTENTIAL.

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Introduction: The family Cucurbitaceae is represented by 125 genera and 960 species, including plants commonly used in people's daily diets (1). Belonging to this family, Cucurbita pepo L., Cucurbita maxima Duchesne, and Cucurbita moschata Duchesne are economically important species that are cultivated worldwide and have high production potential (2). It was stated that extracts prepared from different parts of Cucurbita species, particularly seeds and leaves, have broad pharmacological effects, including antidiabetic, antihypertensive, antitumor, immunomodulatory, antibacterial, antihyperlipidemic, and anti-inflammatory activities (3). The production of C. maxima and C. moschata in Türkiye is based on local cultivars (4). Further, there is only one commercially bred winter squash cultivar (Arıcan 97) (5). Studies on the fruit stems of C. maxima and C. pepo species are very limited. This study aimed to investigate the various biological activities of agricultural wastes from different parts of Cucurbita species.

Materials and Methods: The seed of Arıcan 97 variety of C. maxima was cultivated, and the leaves and fruit stems of the mature plant were collected. The leaves and fruit stems of C. pepo and C. maxima species were obtained from local cultivators. The leaves and fruit stems were shade-dried and powdered in a grinder. All plant materials were extracted with 80% methanol separately. After filtration and solvent evaporation, the crude extracts was fractionated with n-hexane and ethyl acetate, respectively. Acetylcholinesterase, butyrylcholinesterase, tyrosinase, and α-glucosidase inhibitory activities and antioxidant capacity of crude methanol extract, n-hexane, ethyl acetate, and water sub-extracts obtained from the plants were tested by in vitro studies.

Results: C. maxima (Arıcan 97) fruit stem ethyl acetate sub-extract (CMAr97-E), C. maxima (local cultivar) fruit stem ethyl acetate sub-extract, and C. maxima (Arıcan 97) leaf n-hexane sub-extract exhibited noteworthy α-glucosidase inhibitory activity at 200 µg/mL with inhibition percentages of 57.03 ± 1.69%, 50.25 ± 5.41%, and 50.03 ± 5.39%, respectively. CMAr97-E scavenged DPPH radical more strongly than other extracts, with an inhibition percentage of 41.83 ± 1.37% at a concentration of 200 µg/mL. There were no effects of the tested extracts on cholinesterases and tyrosinase enzymes.

Conclusions: The results revealed that the fruit stem of C. maxima (Arıcan 97) has antidiabetic and antioxidant activities. This study indicated that agricultural wastes have the potential to be utilized pharmaceutically. Based on these preliminary findings, we suggest that further biological activity studies should be carried out on agricultural wastes of Cucurbita species, and the compounds responsible for the potential effect should be identified.

Acknowledgements: This study was supported by a grant of TUBITAK (1919B012304519)

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OP046
CHEMICAL COMPOSITION OF ENDEMIC ANTHEMIS ROSEA SUBSP. CARNEA (BOISS.) GRIERSON.

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Introduction: The genus Anthemis L., which belongs to the Asteraceae family, is represented by 35 species and 57 taxa in the flora of Turkey. A. rosea subsp. carnea (Boiss.) Grierson is a widely distributed endemic taxon, known as "Gül papatya" in Anatolia (1). The aim of this study was to determine the chemical composition of A. rosea subsp. carnea collected from nature and cultivated, and to evaluate their differences.

Materials and Methods: Plant materials were collected from Mugla, Burdur and Antalya in May, 2022. Cultivation was carried out in Odemis region, based on results of biological and ecological conditions determined for the plant. The essential oils (EO) and hydrosols of capitulum were obtained by hyrodistillation using Clevenger apparatus and by water-steam distillation using distillery device. Air dried and powdered capitulums were extracted with 70% ethanol in ultrasonic water bath. The chemical compositions of the EO, hydrosols and extracts were investigated using by GC-MS techniques and HPLC analysis, respectively.

Results: GC-MS analysis showed that linalool (21.3-26.7%), α-pinen (7.2-8.2%) and caryophyllene oxide (5.6-7.0%) are the main compounds of the EO's. The whole hydrosols were identified to contain linalool (17.3-65.1%) as the major compounds. HPLC analysis revealed that all extracts contained variable amounts of chlorogenic acid, p-coumaric acid, rutin, hyperoside and apigenin-7-glucoside. Additionally, chlorogenic acid (76.59-354.86mg/100g dry herb) and hyperoside (90.57-195.26mg/100g dry herb) were determined as the main compounds in whole extracts.

Conclusions: This is the first report on chemical composition of the extracts of A. rosea subsp. carnea. This study is a part of a project of product development from A. rosea subsp. carnea.

Acknowledgements: This study was supported by a grant of TUBITAK (TEYDEB 1505, Project number: 521O090).

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OP047
ANATOMICAL STUDIES ON ANKARA ENDEMIC PLANT PRANGOS DENTICULATA FISCH. & C.A. MEY.

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Introduction: Prangos denticulata, known as "dişli çakşır" in Türkiye, is a perennial plant of the Apiaceae family. In Türkiye, the genus Prangos is represented by 22 species, 12 of which are endemic (1,2). P. denticulata has been protected by Baskent University as part of the "Ankara Endemics Conservation Project". Prangos plants have a history of use in Mediterranean and Middle Eastern folk medicine for their wound healing, carminative, hemostatic, and aphrodisiac effects (3). This study examines the detailed anatomical features of P. denticulata, endemic to Ankara and found exclusively in Hüseyin Gazi Hill (2,4).

Materials and Methods: P. denticulata plant material was collected from Hüseyin Gazi Hill, Ankara, in 2022 and is preserved in Herbarium of Ankara University Faculty of Pharmacy (AEF, 30942). Sections from the leaves, stems, and roots were examined in detail under a microscope with sartur and chloral hydrate reagents. Characteristic elements were photographed with a Leica CME.

Results: Cross sections from leaf, stem, and root parts, revealed that the leaf is of the monophasic type and carries 3-5 secretion channels; the stem is U-shaped, with scattered vascular bundles and numerous secretion channels. In the cross section of the root, the presence of 4-10 secretion channels between the pith rays were detected.

Conclusions: With this study, the anatomical structure of the leaf, stem, and root of P. denticulata has been elucidated. These anatomical features will be important for this isolated endemic species.

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OP048
SGLT-2 INHIBITOR EMPAGLIFLOZIN SUPPRESSED SEIZURES AT THE DOSE OF 0.9 µG IN RATS WITH ABSENCE EPILEPSY

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Introduction: SGLT-2 inhibitors, which target the SGLT-2 proteins expressed in the proximal convoluted tubules, are antihyperglycemic drugs (1). One study reports intrahippocampal administration of phlorizine, a specific SGLT inhibitor, excacerbated the pilocarpine-induced seizures (2). The purpose of this study is to investigate the effect of a SGLT-2 inhibitor, empagliflozin (EMPA) on non-convulsive absence seizures in a genetic rat model of absence epilepsy (GAERS).

Materials and Methods: GAERS underwent stereotaxic surgery. Following one-week recovery, rats were intracerebroventricularly injected with either EMPA (0.9 µg, 1.8 µg or 3.6 µg dissolved in saline-DMSO (5%) or saline-DMSO (5%) and their electroencephalograms (EEG) were recorded. Results are presented as mean±SEM, with statistical analysis conducted through two-way ANOVA followed Tukey's post hoc test. The cumulative duration, number, and mean duration of each spike- and- wave discharges (SWDs) were evaluated.

Results: EMPA decreased the cumulative duration, number and mean duration of SWDs in a dose and time-dependent manner. Following injections EMPA suppressed cumulative and mean duration of SWDs at the 40th min [$F(10,143) = 7.26$, $P<0.001$ and $F(10,143) = 4.21$, $P<0.001$], and number of SWDs at the 100th and 120th min [$F(10,143) = 3.795$, $P<0.001$].

Conclusions: These results indicate that SGLT-2 inhibition might be involved in seizure mechanisms in various epilepsy types. Further studies are needed, especially with the lower doses to established more specific effects of EMPA.

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OP049

ROSMARINUS OFFICINALIS ETHANOLIC EXTRACTS RESCUES BV-2 CELLS VIA MODULATING INFLAMMATION AND REDOX BALANCE: COMPARATIVE STUDY WITH CARNOSOL AND CARNOSIC ACID.

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Introduction: Neuroinflammation generally refers to an inflammatory response within the central nervous system caused by various pathological insults, including infection, trauma, ischemia, and toxins (1). Being the sentinel immune cell of the brain, microglia are tasked as the first responders to infection or tissue injury, and initiating an inflammatory response (2). The perennial shrub plant Rosmarinus officinalis L. was reported it has anti-inflammatory, anti-cancer, anti-nociceptive, antidiabetic, neuroprotective, and anti-oxidative properties (3). The present study aimed to investigate the effects of Rosmarinus officinalis ethanolic extracts on the lipopolysaccharide-induced neuroinflammation model of BV-2 cells in the comparison of carnosol and carnosic acid, phenolic diterpenes of the plant.

Materials and Methods: Ultrasound-assisted extraction was used to have ethanolic extract of the plant (4). Lipopolysaccharide (LPS) was used to induce inflammation in BV-2 cells. Tumor necrosis alpha (TNF-α), interleukin 1 beta (IL-1β) secretion, reactive oxygen species (ROS) production, GSH/GSSG ratio, protein carbonyl level, and caspase-3 activity were evaluated.

Results: Inflammation induced by LPS was reduced by the ethanolic extract. Both carnosol and carnosic acid decreased the TNF-α and IL-1β levels as well. The ethanolic extract reduced ROS production and protein carbonylation, and increased GSH/GSSG ratio more effectively compared to the effects of carnosol and carnosic acid. Results depicted that caspase-3 activity was reduced by the ethanolic extract and this effect was more pronounced compared to carnosol and carnosic acid.

Conclusions: The present study indicates ethanolic extract of Rosmarinus officinalis rescues BV-2 cells via alleviating inflammation and oxidative stress.

Acknowledgements: This study was supported by a grant of BAPSİS of Yildirim Beyazit University (TDK-2021-2185)

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Graphics:

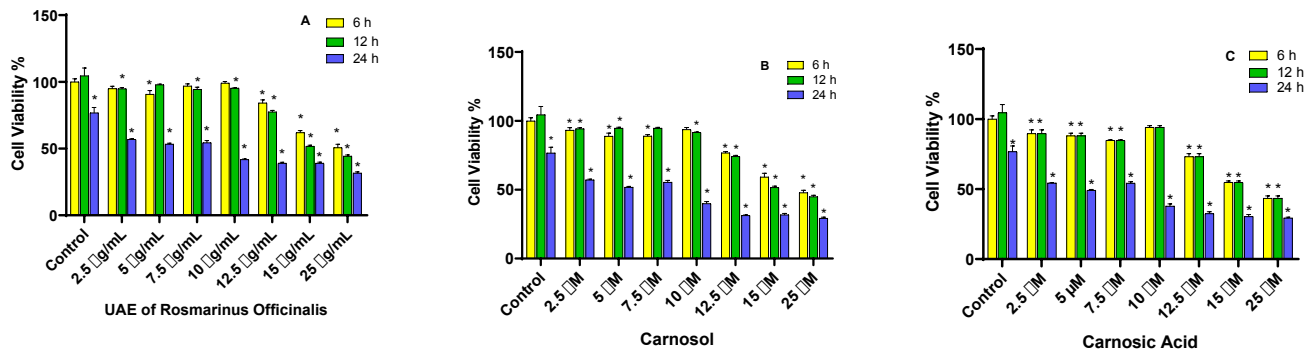

Fig. 1 Changes in cell viability in BV-2 cells when incubated with increased concentrations (2.5 to 25 µg/mL) of UAE of rosemary for 6,12 or 24 h (A, n=4) and Carnosol (2.5 to 25 µM) treatment for 6,12 or 24 h (B, n=4) and Carnosic acid (2.5 to 25 µM) treatment for 6,12 or 24 h (C, n=4) $p<0.05$ compare to control 6 h

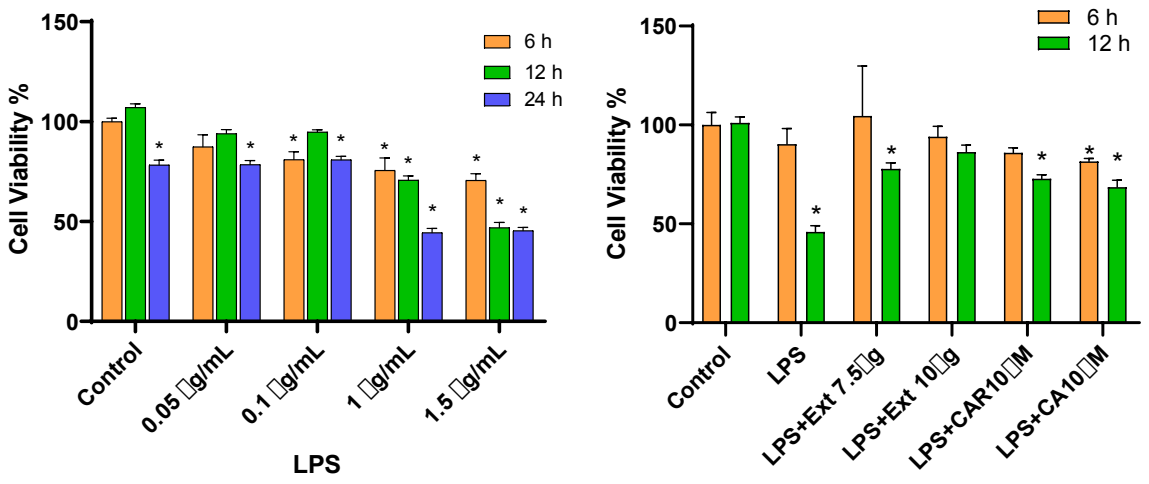

Fig. 2 Determination of LPS, UAE of Rosemary, CAR and CA doses for treatment protocol. LPS (0.05 to 1.5 µg/mL) treatment for 6,12 or 24 h (n=3-4) and LPS+7.5 µg/mL UAE of rosemary, LPS+10 µg/ml UAE of rosemary, LPS+10 µM Carnosol, LPS+10 µM and Carnosic acid treatment for 6 and 12 h (n=3-4). p*<0.05 compare to Control 6 h

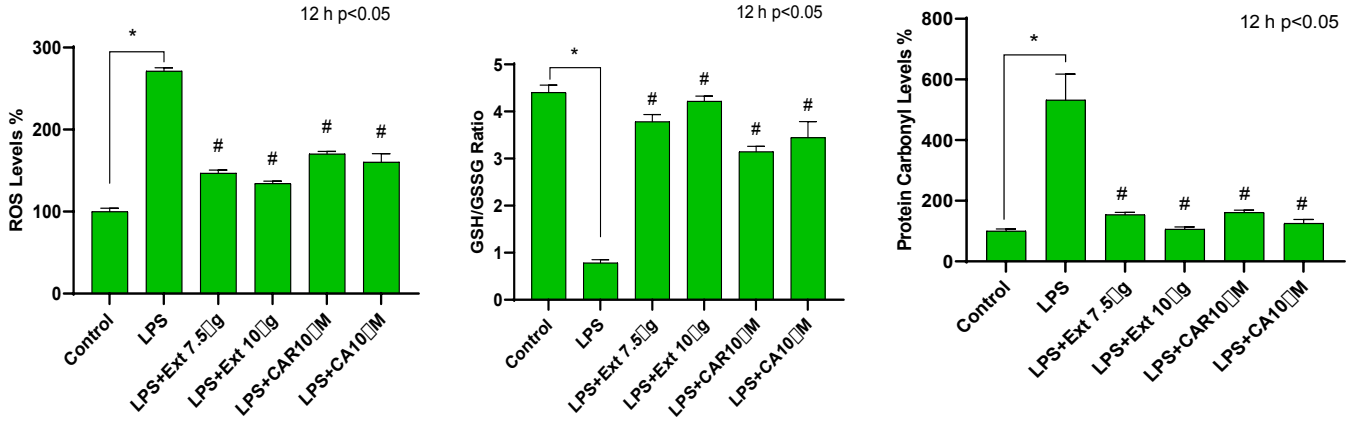

Fig. 3 Evaluation of BV-2 cells for oxidative stress after 12 hours of incubation. LPS: Lipopolysaccharide; CAR: Carnosol; CA: Carnosic Acid; Ext: UAE of Rosemary. p#<0.05 compare to LPS, p*<0.05 compare to Control

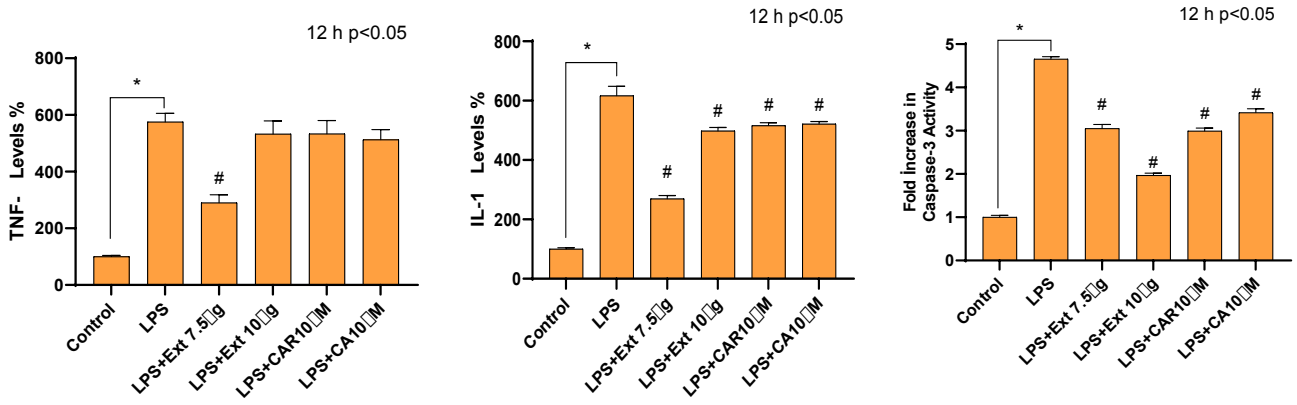

Fig. 4 Evaluation of BV-2 cells for markers of inflammation and caspase-3 activity after 12 hours of incubation. LPS: Lipopolysaccharide; CAR: Carnosol; CA: Carnosic Acid; Ext: UAE of Rosemary p#<0.05 compare to LPS, p*<0.05 compare to Control. Analyzed using one-way ANOVA with Bonferroni test for multiple comparisons.

OP050
THE PREDICTED BIOMARKERS HSA-MIR-1249-5P AND HSA-MIR-320B VIA THE COMMON TARGET GENE PROK2 IN B-CELL APOPTOSIS IN T1DM

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Introduction: Diabetes mellitus (DM) is a chronic metabolic disorder characterized by high blood glucose levels due to insufficient insulin production or resistance to insulin action (1). T1DM, or insulin-dependent DM, is an autoimmune disease where the immune system destroys insulin-producing beta (β) cells in the pancreas (2). Our study employed bioinformatic tools to perform biological pathway-like analyses on statistically significant up-regulated and down-regulated genes in T1DM. Two miRNAs were revealed with a common target gene. Our results suggest that these biomarkers be further studied in vitro and in vivo, focusing on their common target gene to understand the complex pathophysiology of T1DM better.

Materials and Methods: Data sets for mRNA and miRNA expression were investigated on the Gene Expression Omnibus (GEO) database using the keyword 'Type 1 diabetes mellitus.' Initially, the GSE55100 super series, which includes miRNA (GSE55099) and messenger RNA (mRNA) (GSE55098) data sets, was reanalyzed using 'GEO2R.' miRNAs/mRNAs were identified using filters of $|\log2| > 0.58$ and $p=0.05$. mRNAs and miRNAs between T1D and normal samples were identified using filters of $|\log2| > 0.58$ and a p-value of 0.05. The miRDB tool was utilized to predict mRNA targets of the identified down-regulated miRNAs. For the statistically significant up- and down-regulated genes, biological pathway-like analyses were conducted. Focusing on up-regulated genes and genes associated with the inflammation pathway, individual mRNA targets of statistically significant down-regulated miRNAs in the GSE55099 miRNA data were identified using the miRDB tool. Pathway analyses were then performed on these target genes, focusing on genes enriched in the set of up-regulated genes among the targets of each miRNA, particularly those involved in inflammation.

Results: hsa-miR-1249-5p and hsa-miR-320b were revealed with their common target gene PROK2.

Conclusions: Increased inflammation and immune activation are key features of T1DM (3). miR-1249-5p and miR-320b may modulate immune responses as they regulate inflammatory responses, insulin secretion, and apoptosis (4,5). Dysregulation of these miRNAs could affect the expression of the common target gene PROK2 involved in the autoimmune attack on pancreatic β cells. Understanding the specific contributions of these miRNAs in T1DM can provide insights into disease mechanisms and identify potential targets for therapeutic intervention. Further research is needed to elucidate their precise roles and therapeutic potential in the context of T1DM.

Acknowledgements: This study was supported by a grant from TUBITAK (TEYDEB-7238013)

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OP051
MICROBIOLOGICAL ACTIVITIES OF FOUR HERACLEUM L. SPECIES

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Introduction: Heracleum L. genus of the Apiaceae family, have about 125 species; fourteen species grow naturally in Turkey, among these seven of them are endemic (1). In traditional medicine, Heracleum species are used as antipyretic, analgesic, antiseptic, carminative, diaphoretic, digestive and as a flavoring agent and spice for foods for rheumatic disease, gastralgia, and injuries from falls, fractures, contusions and strains. Pharmacological studies showed that Heracleum and its active compounds have various biological activities, particularly anti-inflammatory, anticonvulsant, antifungal, anticancer, anti-psoriatric, anti-vitiligo and antioxidant activities (2).

This study aims to evaluate the antimicrobial, antibiofilm, and anti-quorum sensing (anti-QS) activities of extracts prepared from four *Heracleum* species.

Materials and Methods: Methanolic extracts were prepared from the roots and herbs of H. pastinacifolium subsp. incanum, H. crenatifolium, H. sphondylium subsp. montanum, H. paphlagonicum species belonging to the Heracleum genus by maceration. After evaporating to dryness, antimicrobial analysis was performed on the solution prepared with 5% Dimethylsulfoxide (DMSO) with a concentration of 40 mg/ml. The broth microdilution method was used to determine the MIC (Minimum Inhibitory Concentration) values of the extracts. Using the crystal violet assay, the antibiofilm activity was determined by in vitro microplate-based biofilm model against *Pseudomonas aeruginosa* PAO1. The anti-QS activity test was conducted using the disc diffusion method with the reporter bacteria *Chromobacterium violaceum* ATCC 12472.

Result and Conclusion: Among the tested extracts, H. pastinacifolium (herba) showed the best antimicrobial activity. The extracts showed better antibacterial activity against Gram-positive bacteria. However, none of the extracts were found to exhibit antibacterial activity against Klebsiella pneumoniae ATCC 13383 or P. aeruginosa ATCC 27853. These observed activities can be considered weak compared to standard antimicrobials (ciprofloxacin, gentamicin, fluconazole). Among the tested extracts, H. pastinacifolium (herba) showed the highest antibiofilm activity, with a biofilm inhibition value of 73.21%. No anti-QS activity was observed for violacein production by any of the tested extracts.

Key Words: *Heracleum*, antimicrobial activity, antibiofilm activity, anti-quorum sensing activity

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OP052
ANTIBIOFILM ACTIVITY OF CSA-44 AND CSA-192 AGAINST VANCOMYCIN RESISTANT ENTEROCOCCUS

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Introduction: Enterococcus spp. are Gram-positive bacteria that are mainly commensal members of the gastrointestinal tract and can cause various infections. Bacteremia, endocarditis and urinary tract infections are the main infections they cause. Their success in developing antimicrobial resistance and their ability to form biofilms make the treatment of these infections challenging. Today, increasing rates of antibiotic resistance in enterococcus, particularly vancomycin-resistant enterococcus (VRE), make these organisms critical. Therefore, attempts have been made to discover new antimicrobial agents that can prevent resistance and target planktonic and biofilm forms. Cationic steroid antibiotics (CSA), designed to mimic the activities of antimicrobial peptides, are a new class of antimicrobial agents (1,2). The aim of this study was to determine the effect of CSA-44 and CSA-192 on different stages of Enterococcus spp. biofilm formation.

Materials and Methods: Primarily Enterococcus spp. strains (17 of them VRE) biofilm formation was confirmed in 96-well polystyrene microtitre plates and then minimum inhibitory concentrations (MIC) results of CSAs were evaluated. MIC50 and MIC90 values for both CSAs were found 2 and 4 µg/ml respectively in our previous study (3).

In this study the in vitro activities of CSA-44 and CSA-192 were investigated against adhesion (for 1, 2 and 4 hours with 1/10 x MIC) and biofilm formation (for 24 hours with 1 x MIC, 1/10 x MIC and 1/100 x MIC) of fifty Enterococcus spp. strains isolated from various clinical samples from Synevo Laboratories Ankara Central Laboratory (4). In addition, the effects of different concentrations (16, 32, 64, 128 and 256 µg/mL) of CSA-44 and CSA-192 on mature biofilms of Enterococcus spp. were investigated by MTT method (5).

Results: Although inhibition of adhesion and biofilm formation rates depended on time and concentration, it was found that percentage inhibition of adhesion rates for CSA-44 was 18.18 and for CSA-192, 20.91. It was also found that inhibition rates of biofilm formation for CSA-44, 37.12 and for CSA-192, 39.31. CSA-44 was found more effective than CSA-192 on mature biofilms of Enterococcus spp. and it reduced the number of biofilm cells by half even at 32 µg/mL.

Conclusions: Enterococcus spp., especially VRE, is known to be a major cause of healthcare-associated infections worldwide. The eradication of biofilms is also very important in the control of infections. In this regard, the results of our study reveal that CSA-44 and CSA-192 can be used as an alternative to conventional antibiotics for the eradication of Enterococcus spp. biofilms.

Keywords: *Enterococcus spp.,* Vancomycin-resistant *Enterococcus*, biofilm, cationic steroid antibiotics

Acknowledgements: This research was funded by Health Institutes of Türkiye (TUSEB) (A Grubu Acil Ar-Ge Proje Destek Programı, Project number: 12093).

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OP053
DETERMINATION OF THE OPTIMAL CONCENTRATION OF A PHAGE-ANTIBIOTIC COMBINATION AGAINST RESISTANCE PSEUDOMONAS AERUGINOSA STRAİNS.

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Introduction: Although strategies involving the combined use of two or more antibiotics have been developed to combat resistance, the number of multidrug-resistant or pan-drug-resistant strains is increasing every day. The use of phages, which naturally kill bacteria, is not a new approach. However, it has become more focused due to increasing resistance (1). In our study, we tested the efficacy of phage in combination with ceftazidime or tobramycin on resistant Pseudomonas aeruginosa (P. aeruginosa) isolate was tested.

Materials and Methods: The bacteriophage–antibiotic interactions were examined using the checkerboard assay (2). In this study, the interactions of previously isolated lytic Pseudomonas phage vB_Pa46, vB_Pa73, vB_Pa81 with tobramycin or ceftazidime were determined. Two-fold serial dilutions of ceftazidime or tobramycin (0.25–128 µg/mL) at horizontal rows and each phage separately (1012-103 PFU/mL) at vertical rows were prepared in sterile the 96-well plate. The synergy between antibiotic and phages was quantified by determining the fractional inhibitory concentration index (FICi) was calculated.

Results: As a result of the study, the minimum inhibitory concentration (MIC) value of ceftazidime for P30 bacteria decreased from 32 to 8 with each phage-antibiotic co-administration. The FICi value was calculated to be between 0.25-0.406. The MIC value of tobramycin for P30 bacteria decreased from 256 to 8, 16 and 4 with the co-administration of antibiotic F46, F73 and F81 phage, respectively. The FICi value was calculated as 0.062, 0.0125 and 0.0218 respectively. In both antibiotic classes, the F81 phage is the most effective at low concentrations.

Conclusions: In our study, the synergy is detected with all phages and tobramycin or ceftazidime against P. aeruginosa. With the development of phage-antibiotic co-use strategies, it is seen that their use at low concentrations is an effective approach to prevent the development of resistance and therefore this combination is thought to be an effective way to therapy.

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OP054
INVESTIGATION OF SIDEROPHORES OF CLINICAL ACINETOBACTER BAUMANNII ISOLATES USING CAS-AGAR AND CAS-LIQUID TEST

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Introduction: Microorganisms form some organic compounds called siderophores to survive in low iron concentrations. Siderophores are low molecular weight, metal-chelating substances that capture insoluble ferric iron (Fe+3) from different environments (1). Siderophores are non-ribosomal peptides generally produced by microorganisms such as bacteria and fungi. The iron-binding ability of siderophores can be used in many areas, such as medicine and agriculture. Siderophores have the potential to be utilized as carriers of drugs for treating antibiotic-resistant bacteria. The iron transport abilities of siderophores are used to transport the antibiotic into the cell. This strategy, known as the "Trojan horse strategy," aims to prevent resistance mechanisms by reducing cell membrane permeability by preparing conjugates of siderophores with antimicrobial compounds (2). This study aims to investigate the siderophore production of A. baumannii isolates using CAS-Agar and CAS-Liquid Tests.

Materials and Methods: In this study, 48 clinical A. baumannii isolates were used. The siderophore production of A. baumannii isolates was examined using CAS-Agar and CAS-Liquid Tests (3,4,5). A. baumannii ATCC 19606 strain was used as a positive control. In the CAS-Agar test, the color of the medium turns yellow-orange, indicating that the bacteria produce siderophores. In the Cas-Liquid test, the % siderophore unit was calculated by performing measurements at 620 nm using a spectrophotometer.

Results: In the Cas-Agar test, the isolates exhibited different degrees of color change in the medium, which depended on the siderophores they produced. In the CAS-Liquid test, it was observed that the isolates produced siderophores better at 37 °C than at 30 °C.

Conclusions: Both methods can detect siderophore production in clinical isolates. In the Cas-Liquid test, some isolates produced more siderophores at 37°C.

Acknowledgments: This study was supported by the Ankara University Scientific Research Council (21L0237003). BIDEB/2211-A Doctoral Program, Turkish Technological Research Council (TÜBİTAK) provided financial support.

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OP055
ANTIMICROBIAL ACTIVITIES OF ESSENTIAL OILS OF SOME SALVIA SPECIES

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Introduction: Antibiotic resistance is a significant problem in modern medicine, and natural products hold promise in addressing this issue. Herbal natural products may contain components with antibacterial properties, which can be effective in combating bacteria resistant to antibiotics. In this regard, essential oils are notable for their potential in the treatment of bacterial infections.

The Lamiaceae family includes well-known aromatic plants like oregano, thyme, basil, and sage. *Salvia* L. is the largest genus of Lamiaceae, consisting of around 1000 species worldwide. It has more than 100 species in Türkiye and is known as 'sage' in Anatolia [1,2].

Materials and Methods: This study was conducted on the essential oils of *Salvia aucheri* subsp. *canescens* (Boiss. & Heldr.) Celep, Kahraman & Doğan, *S. heldreichiana* Boiss, and *S. aytachii* Vural & Adıgüzel plants, which grow naturally in Turkey. To evaluate antimicrobial activity, the following test bacteria were used: *Escherichia coli* ATCC 25922, *Klebsiella pneumoniae* ATCC 13883, *Pseudomonas aeruginosa* ATCC 27853, *Staphylococcus aureus* ATCC 25923, and *S. aureus* ATCC 43300 (methicillin-resistant strain). The essential oil prepared in %10 DMSO and %0.05 Tween 80, and minimum inhibitory concentration (MIC) values were determined using the broth microdilution method [3].

Results: In GC-FID and GC-MS systems results; α-Pinene (9.5, 13.1, 4.3%), 1,8-cineole (21.2, 9.1, 20.0%), camphor (19.1, 1.7, 20.3%) and borneol (6.0, 6.4, 5.0%) were determined as main components for S. aucheri subsp. canascens, S. heldreichiana, S. aytachii, respectively [1,2]. The highest antimicrobial activity was observed with S. aucheri essential oil against Staphylococcus aureus ATCC 25923 with a MIC value of 1,56 mg/ml. S. heldrichae and S. aucheri essential oils more effective than S. aytachii essential oil against S. aureus ATCC 43300.

Conclusions: It is thought that the antimicrobial activity of the essential oils may be due to the main components, 1,8 cineole, camphor, and pinene. However, the observed activity was considered weak when compared to control antibiotics.

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OP056
GREEN SYNTHESIS AND CHARACTERIZATION OF ZINC NANOPARTICLES USING MACLURA POMIFERA (RAFİN.) SCHNEIDER AND THEIR ANTIBACTERIAL, ANTIBIOFILM AND ANTI-QUORUM SENSING ACTIVITIES

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Introduction: Maclura pomifera (Rafin.) Schneider is generally known as Osage orange and is rich in phenolic compounds. (Altuner et al. 2012). Green synthesis methods are non-toxic and cost-effective compared to other methods. (Gour and Jain, 2019). The aim of this study is to synthesize and characterize zinc nanoparticles (ZnNPs) using Maclura pomifera. Then, the antibacterial activity, antibiofilm and anti-quorum sensing (anti-QS) activities of the synthesized nanoparticles were investigated.

Material and Method: Ethanolic extract was prepared from *Maclura pomifera* fruits. The extract was added to the $ZnCL_2$ solution.It was incubated and centrifuged. Characterization studies were performed using UV-Vis, FTIR, XRD, and SEM. For the antibacterial activity, the MIC values of the nanoparticles were determined using the broth microdilution method. The anti-QS activity test was performed by the disc diffusion method.The antibiofilm activity against *P. aeruginosa* PAO1 was evaluated using the crystal violet assay (Junejo et al., 2023).

Results: From the UV-visible spectrum, the peak of ZnNPs was observed to occur at 360nm. SEM analysis showed that the particle size was less than 100nm. The ZnNP exhibited the best antibacterial activity against S. aureus ATCC 25923, with an MIC value of 0,25 mg/ml.In the anti-QS activity test, it was observed that ZnNP had a weak inhibition zone. The percentage biofilm inhibition value of ZnO NP was determined as 46.42%.

Conclusions: The characterization results indicate that the nanoparticles were synthesized successfully. Furthermore, ZnNPs appear to have three activities.

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OP057
RECENT MARKETING TRENDS IN PHARMACEUTICAL INDUSTRY

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Introduction: The concept of marketing has changed over the years and differs according to recent developments (1). One of the most important influences here is the changing behavior of consumers with a change in information-communication technologies. This study aimed to examine the marketing trends reflected in the literature over the last five years in marketing activities in the pharmaceutical market.

Materials and Methods: Marketing and social marketing trends in the pharmaceutical market were evaluated according to the literature published in the last five years from electronic databases (Scopus, PubMed and Web of Science) using the keyword "pharmaceutical industry marketing".

Results: In the studies examined within the scope of this study, studies that can be evaluated in terms of integrated marketing communication come to the fore. Within the scope of Business-to-Business (B2B) and Direct-To-Customer (DTC), the digitalization of marketing channels, the impact of developing technology on marketing, and activities that are in line with sustainability stand out.

Conclusions: Marketing activities that differ according to the legislation of the countries emphasize the increasing impact of new opinion leader influencers, who operate to influence consumers' usage habits, on marketing activities in the pharmaceutical market, even though in some countries they may not be carried out directly to the consumer (2). In the other hand, social marketing activities are also remarkable (3). However, it is important that sustainability and the impact of digital tools on marketing are addressed in terms of human health and ethics.

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OP058
DETECTING DRUG-DRUG INTERACTIONS INDUCED BY ANTI-HYPERLIPIDEMICS: AN OBSERVATIONAL STUDY

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Introduction: Dyslipidemia is a clinical condition that is encountered most frequently both in Türkiye and worldwide, and it is also one of the most important risk factors for cardiovascular diseases (1,2). While lifestyle changes play a significant role in the treatment of dyslipidemia, pharmacological therapy is often necessary. Hence, this study aimed to reveal drug-drug interactions (DDIs) due to antihyperlipidemic drugs through programs used to detect DDIs.

Materials and Methods: Within the scope of this study, 250 prescriptions containing at least one anti-hyperlipidemic drug and a drug from a different pharmacological group were evaluated in terms of DDIs between November 2022 and April 2023. Evaluations were made on the prescriptions received in a community pharmacy serving in Van. Three different DDI checking programs (RxMediaPharma®, Medscape, and Drugs.com) were used for this evaluation.

Results: Anti-hyperlipidemic drug-induced DDIs were detected in 115 of the prescriptions. DDIs occurred between 38 active ingredient pairs. It was determined that 85% of the interactions were caused by atorvastatin. The most common DDI was found between atorvastatin and pantoprazole. This interaction is at a level that needs to be monitored and was detected by all three databases. Another common interaction was found between atorvastatin and clopidogrel, which was detected at the "moderate" level in only one database. Finally, when the databases used to detect DDIs were considered, it was determined that the three databases gave different results. For only 7 of 38 different ingredient pairs, all three programs gave the result that there was an interaction.

Conclusions: As a result, DDIs induced by anti-hyperlipidemic drugs generally were found to be at moderate levels. However, it is seen that three DDI checking programs used in the study provide different results in detecting DDIs. This study emphasizes the necessity for further research on DDIs. Determining drug interactions with more precise and consistent data can contribute to the development of safer and more effective treatment strategies.

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OP059
DETECTION OF DRUG-DRUG INTERACTIONS CAUSED BY ANTI-HYPERTENSIVES: AN OBSERVATIONAL STUDY

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Introduction: Hypertension is increasing in our country and the world, and it accompanies many chronic diseases (1). In hypertension, where pharmacological agents are generally preferred in the treatment, factors such as additional diseases and age increase the frequency of polypharmacy (multi-drug) use in patients. An increase in the possibility of drug-drug interactions accompanies this situation. In this regard, this study aimed to reveal drug-drug interactions (DDIs) due to antihypertensive drugs through programs used to detect DDIs.

Materials and Methods: Within the scope of this study, 325 prescriptions containing at least one antihypertensive and a drug from a different pharmacological group, filled in a community pharmacy serving in the city center of Diyarbakir, were evaluated in terms of DDIs between November 2022 and April 2023. Three different DDI checking programs (RxMediaPharma, Medscape, and Drugs.com) were used for this evaluation.

Results: Antihypertensives-induced DDIs were found in 232 of the prescriptions. When the detected DDIs were evaluated on a group basis: (i) 254 of the DDIs were due to beta blockers and occurred between 88 different active ingredient pairs, (ii) 73 of them were due to ACE inhibitors and occurred between 38 different active ingredient pairs, (iii) 113 of them were due to calcium channel blockers and occurred between 42 different active ingredient pairs, (iv) 128 of them were due to ARBs and occurred between 55 different active ingredient pairs, (v) 250 of them were due to diuretics and occurred between 93 different active ingredient pairs, and (vi) 7 of them were due to alpha blockers and occurred between 5 different active ingredient pairs. DDIs were mainly detected between metoprolol and aspirin. All three databases simultaneously gave an interaction warning for only 61 active ingredient pairs.

Conclusions: It has been found that the frequency of antihypertensive-related drug interactions is high and that they cause interactions at different levels, from minor to serious. However, it is seen that three DDI checking programs used in the study provide different results in detecting DDIs. Determining DDIs with more precise and consistent data can contribute to developing safer and more effective treatment strategies.

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OP060
PREFERENCES AND UTILIZATION OF MOBILE APPLICATIONS IN OLDER ADULTS

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Introduction: Health-based mobile applications can support patients' health through individualization, compatibility with body-worn sensors and real-time information exchange, especially for those who have chronic diseases. More than fourteen thousand self-management mobile applications can be downloaded for health-related support (1). However, the highest-rated health applications were lacking of basic functions such as helping older adults organize their medication regimens and checking medications (1). This study aims to determine the preference and utilization of mobile applications in older adults.

Materials and Methods: This was a multicenter study conducted in hospital and community pharmacy settings. The survey included 15 questions about the preferences and utilization habits of mobile applications. It was implemented among patients who were 60 years or older and voluntarily accepted to participate in the study.

Results: A total of 296 respondents with a mean (standard deviation) age of 72.54 (7.59) participated in the study. A few had university or higher degrees (17%) while the majority took their medications without any support (94%). More than half of the respondents indicated that they had at least one mobile application downloaded to their smart phone (69%) and %36 indicated at least one of their mobile applications was related to health. They agreed or strongly agreed that technical features such as performance (68%), clinical features such as the reliability of the information provided (%60), recommendation from the physician or pharmacists (64%) and cost (79%) affect their utilization of mobile health applications.

Conclusions: The results of this study demonstrated that there was a high tendency to use mobile applications in older adults and the features of mobile applications could affect their utilization. It was revealed that older adults took their medications themselves, which may increase the risk of poor medication adherence. Considering the unique needs and special characteristics of older adults, it is crucial to design a mobile health application that fits well with the older population. A well-developed mobile health application can support to improve and maintain medication adherence among older adults.

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OP061
POTENTIAL ANTI-INFLAMMATORY EFFECT OF CANNABIDIOL ON THE OFFSPRING OF SYSTEMIC INFLAMMATION-INDUCED PREGNANT RATS

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Introduction: Natural compounds obtained from plants have been widely used for various conditions due to their potential anti-inflammatory, anti-oxidant, anti-bacterial and anti-tumor activities (1). Also, studies demonstrated their neuroprotective roles in the treatment of neurodegenerative diseases (2). Cannabis sativa is a popular plant that has been used medicinally since ancient times. Pharmacotherapeutic approaches have led to the search for phytocannabinoids and their effects on the human body (3). The potential protective roles of cannabinoids have been demonstrated in various conditions, including chronic pain, multiple sclerosis, epilepsy and Parkinson's disease (4). Cannabidiol (CBD) is one of the most abundantly found phytocannabinoids in the Cannabis sativa and it is extensively used in many medical conditions due to its lack of psychotic properties (5). In the present study, we aimed to investigate the possible anti-inflammatory effect of CBD in a rat model of systemic inflammation in pregnancy, which is one of the underlying factors of preterm birth.

Materials and Methods: 12 weeks adult female Wistar albino rats (n=30) mated 15 male rats for a week. Routine vaginal smear tests were performed to confirm pregnancy. Pregnant rats (n=30) were divided into five groups; control, LPS (lipopolysaccharide, i.p.), LPS+ CBD 5 mg/kg (i.p.), LPS+ CBD 10 mg/kg (i.p.) and LPS+ CBD 30 mg/kg (i.p.). After the injections, blood samples of rats were collected and fetuses were taken by hysterectomy. Thereafter, fetal brain tissues were removed and further analysis was conducted, including immunohistochemical staining, ELISA and immunoblotting analysis to examine inflammatory parameters. All animal care and experimental procedures were conducted following the guidelines for animal research from the National Institutes of Health and were approved by the Committee on Animal Research at Suleyman Demirel University, Isparta (Ethic No: 17.06.2021 01/05).

Results: Our histopathological findings demonstrated that CBD administration decreased congestion, edema and hemorrhage compared to the LPS-treated group. Immunohistochemical staining results showed that CBD significantly decreased tumor necrosis factor-alpha (TNF-α) expression levels in fetal brain tissues compared to the LPS-treated group. These findings related to this inflammatory response were also supported by serologic results and IL-1β concentrations in fetal brain tissues decreased in CBD-treated groups compared to the LPS group. Additionally, immunoblotting assay indicated that CBD treatment significantly suppressed the nuclear factor kappa B (NF-κB) activation compared to the LPS-treated group.

Conclusions: The present study suggests that CBD can be an alternative therapeutic option to avoid inflammatory conditions that could negatively impact the fetal brain during pregnancy due to its anti-inflammatory effects.

Acknowledgements: This study was supported by Suleyman Demirel University internal funds (TDK-2021-8396).

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OP062

THE IMPACT OF A HIGH FRUCTOSE DIET ON ERECTILE DYSFUNCTION IN RATS WITH BILATERAL CAVERNOUS NERVE INJURY

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Introduction: Metabolic syndrome (MetS) is a collection of many risk factors, including insulin resistance, high blood glucose, and hypertension. Consuming an excessive quantity of fructose may raise the risk of developing MetS. Researches imply a cause-and-effect relationship between MetS and erectile dysfunction (ED). ED, a common complication of pelvic procedures such as radical prostatectomy (RP), is caused by cavernous nerve damage. The cavernous nerves play a vital role in beginning penile erections. Patients with MetS who have radical prostatectomy (RP) are likewise more likely to develop ED. MetS causes insulin resistance, linked to nerve injury and reduced neuron regeneration. This research aimed to assess MetS's impact on ED in a rat model with bilateral cavernous nerve injury (BCNI).

Materials and Methods: A total of 32 adult male Wistar Albino rats (n=32) were studied in four groups: 1) Sham-operated control rats, 2) BCNI-induced rats, 3) fructose-treated (10 % in drinking water, 1 month)-rats and 4) fructose-treated and BCNI rats. An intraperitoneal glucose tolerance test was performed to evaluate if animals have MetS and insulin resistance. *In vivo,* erectile responses obtained by stimulation of the cavernosal nerves were expressed as intracavernosal pressure (ICP)/mean arterial pressure and total ICP. *In vitro,* relaxant responses using organ baths were measured. Western blot and immunohistochemistry analyses were used to determine the expression and localization of endothelial nitric oxide synthase (eNOS), neuronal nitric oxide synthase (nNOS), transforming growth factor-beta (TGFβ)-1, hypoxia-inducible factor-1 alpha (HIF-1α). The ratio of smooth muscle to collagen and nerve degeneration was calculated using Masson's trichrome.

Results: Rats with MetS showed a reduced erectile response, worsened by BCNI. BCNI rats had decreased acetylcholine and electrical field stimulation in corpus cavernosum strips. MetS further reduced eNOS and nNOS while increasing TGF-β1 and HIF-1α gene levels in BCNI rats. MetS also increased TGF-β1 protein expression and decreased nNOS protein, partially reducing smooth muscle mass, with BCNI amplifying this effect.

Conclusions: Neurogenic and endothelium-dependent relaxation responses are reduced by MetS, which is detrimental by causing inflammation to erectile responses with BCNI. BCNI with high fructose consumption and cavernous nerve damage contribute more to the development of MetS The mechanisms regarding the interaction of inflammatory mediators with each other and causing MetS and eventually ED, require further understanding. Targeting TNF-α in preventing the progression of MetS associated ED may be a promising novel strategy in this regard. Certainly, these results strengthen the quality management of ED linked RP with MetS and will facilitate drug innovation and more extensive research on other contributing factors could help clarify the results.

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OP063
VENETOCLAX TARGETS HUMAN NEUROBLASTOMA CELLS VIA ALTERATION OF IRON HOMEOSTASIS AND LIPOTOXICITY.

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Introduction: Neuroblastoma is among the most widely diagnosed extracranial pediatric tumors. Despite the available treatment options, low survival rates necessitate alternative treatment approaches, especially for the high-risk patients (1). Venetoclax (VTX) is an inhibitor of anti-apoptotic protein Bcl-2, which has originally been approved by FDA for leukemia. Recent data suggest that it may have a promising antitumor behavior against neuroblastoma, however its underlying mechanisms are yet to be deciphered (2). In the present study, the therapeutic potential and the role of VTX in iron homeostasis were investigated in neuroblastoma cells.

Materials and Methods: The viability of human neuroblastoma (SH-SY5Y) and L929 healthy cells treated with VTX single or combined with ferroptosis inhibitors (deferoxamine, ferrostatin-1) and antioxidants (n-acetylcysteine, mannitol) was measured by the MTT assay. ROS generation was detected with DCFHDA staining. Furthermore, intracellular labile iron pool and lipid accumulation were visualized with confocal microscopy by Hoechst/Calcein-AM/Neutral Red triple staining.

Results: Results have demonstrated that single treatment of 25 µM VTX reduced the SHSY-5Y cell viability to 54,70±4,94 (%), whereas in healthy L929 cells it was determined as 75,07±7,73 (%) ($p<0.05$), indicating partial selectivity. Time-dependent viability analyses revealed that the toxic behavior of VTX starts at 6 h, where elevated ROS generation was observed. Moreover, labile iron-mediated lipid accumulation increased significantly. Interestingly, these effects were reversed in the presence of ferroptosis inhibitors and mannitol, indicating ferroptotic cell death ($p<0.05$).

Conclusions: In conclusion, the findings of the present study demonstrated for the first time that VTX alters iron homeostasis and causes lipotoxicity in human neuroblastoma cells, making it a promising therapeutic approach.

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OP064
DEVELOPMENT AND VALIDATION OF A SENSITIVE ANALYTICAL METHOD FOR DEXAMETHASONE PHOSPHATE RESIDUE DETERMINATION

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Introduction: Dexamethasone sodium phosphate (DxP) is the water-soluble derivative of dexamethasone. DxP is an ester of dexamethasone used to treat a variety of conditions (1). In this study, it is aimed to establish and validate an analytical method for the quantification of DxP residues on the various surfaces of manufacturing equipments within the comcept of cleaning validation to prevent potential cross-contamination (2,3).

Materials and Methods: Surface sampling was conducted via direct swabbing from stainless steel and glass surfaces samples representing the manufacturing equipment surface. Concurrently, rinse sampling methodologies were evaluated for the analysis of inlet sticks, sampling valves, and needle sets. Preparation of swabs involved their saturation in ultrapure water, while rinse samples were systematically diluted with ultrapure water prior to their chromatographic injection. Chromatographic separation was achieved using a reverse-phase HPLC, utilizing a Phenomenex Kinetex EVO C18 column (100 Å 100x4.6 mm, 2.6 µm). The elution was performed with a mobile phase consisting of potassium dihydrogen phosphate buffer and methanol in equal volumetric proportions (50:50 v/v), at a flow rate of 1.0 mL/min. Detection was carried out with a UV detector at 242 nm. The analytical column was thermostated at 40°C, and the injection volume was set at 100 µL. The method demonstrated a total run time of 10 minutes. The method was validated in accordance with the ICH guideline (4).

Results: The method exhibited no interference from placebo, diluent, swab sticks, or surfaces. Linearity was demonstrated within the range of 0.003-0.9 ppm, with a regression coefficient of 0.9981. The LOD and LOQ were determined to be 0.0002 ppm and 0.0006 ppm, respectively. Recovery factors were calculated as 1.53 for stainless steel surfaces, 1.47 for glass surfaces, 1.23 for inlet sticks, and 1.41 for sample valves. The analytical method yielded results that were within the accuracy and precision limits specified by ICH guidelines. The optimized sampling methods achieved a recovery rate exceeding 65%, ensuring reliable detection of DxP residues.

Conclusions: This study confirms that the developed and validated sampling and analytical methods are effective for determining DxP residues in the concentration range of 0.003-0.9 ppm on sterile production equipment surfaces. These methods ensure compliance with stringent cleaning validation requirements, thereby maintaining product quality and safety in regard to cross contamination.

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OP065
ELECTROCHEMICAL DETECTION OF INTERACTION BETWEEN DSDNA AND GLYPHOSATE

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Introduction: Glyphosate, a widely used broad-spectrum herbicide effective on both broad-leaf and narrow-leaf plants, has been classified by the IARC as "possibly carcinogenic to humans" (Group 2A), highlighting its potential health risks (1). Depending on the dose and application methods, Glyphosate can cause skin and eye irritation, respiratory problems, and immune system problems, disrupting the production and function of hormones in the endocrine system (2).

Electrochemical mechanisms, crucial for all redox chemistry, including biological systems related to electron transport chains, play a significant role in protecting human health. They can measure substances that may adversely affect human health and detect DNA damage. Investigating DNA-herbicide interactions is of great importance in understanding the mechanism of action of pesticides on DNA. The aim of this study is to elucidate the interaction mechanism of glyphosate and dsDNA.

Materials and Methods: The electrochemical experiments were conducted using the AUTOLAB-PGSTAT 30 electrochemical analysis system. The electrochemical cell with a 3.0 mm diameter glassy carbon (GC) working electrode, a platinum wire counter electrode, and an Ag/AgCl (3 M NaCl) reference electrode were used. Glyphosate and calf thymus (ct)- dsDNA, both supplied from Sigma-Aldrich. Glyphosate stock solutions of 3400 ppm and dsDNA stock solution of 500 ppm were prepared in ultra-pure water and stored at +4 °C. pH 4.7 acetate buffer solution used as a supporting electrolyte.

Results: The electrochemical interaction between glyphosate and dsDNA was investigated by differential pulse voltammetry (DPV) in the solution phase. The interaction of glyphosate with ct-dsDNA were tested at 20 ppm to 100 ppm glyphosate concentrations and 0-, 2- and 3- incubation times. The changes of peak currents of deoxyguanosine (dGuo) and deoxyadenosine (dAdo) were recorded in solution with only 100 ppm dsDNA, only glyphosate and the mixture of dsDNA and glyphosate at 0-, 2- and 3-hour time intervals. After interaction, the electrochemical signals of dGuo and dAdo were significantly decreased with a mixture of 100 ppm Glyphosate and 100 ppm dsDNA at 2 hours. The interaction between glyphosate and dsDNA was compared with electrochemical DNA biosensors and spectroscopic methods.

Conclusion: The observed changes in the peak currents of the dGuo and dAdo, directly proportional to the increase in the between 20 ppm to 100 ppm Glyphosate concentrations, underscore the importance of our proposed method.

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OP066
DESIGN OF MOLECULARLY IMPRINTED POLYMERS: THE SELECTION CRITERIA OF FUNCTIONAL MONOMER FOR SELECTIVITY

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Introduction: Molecularly imprinted polymers (MIPs) are artificial receptors with specific three-dimensional recognition sites in a synthetic polymer network. The recognition sites include multiple specific binding sites with shape, size, and functional groups to the target molecules formed in polymers (1). One of the critical steps in the design of molecularly imprinted polymer is the choice of functional monomer because its directional interactions with template molecules are required to form molecular imprints that serve as selective recognition sites for template (2). The functional monomer interact strongly with the template molecule via non-covalent interactions (hydrogen bonding, ionic interactions, van der Waals forces, etc.) or covalent interactions. The strength and type of these interactions are crucial for forming a stable pre-polymerization complex. Especially, pseudospecific ligands can be also used to recognize a wide range of biomolecules. Molecularly imprinted techniques using pseudospecific ligand can be favorable in much cases. Small aminoacid-molecules can be used as pseudo-specific ligands and may hold certain advantages as ligands for industrial bioaffinity separations since they are not likely to cause an immune response in case of leakage into the product (3). Therefore, in our studies aminoacid based functional monomer has been synthesized and used as a pseudo-specific ligand in regarding to interested analyte. Pseudospecific ligands interacts through its carboxyl, amino, phenyl and imidazole groups with several templates at around their functional groups and has shown particular efficiency in detection, separation and purification of molecules. Moreover, this improve the selectivity for the design and synthesis of a new materials that cooperatively develop molecular imprinting methodologies. By carefully selecting the functional monomer, it is possible to create highly selective and efficient MIPs tailored for specific applications, such as sensors, drug delivery systems, or separation processes. Thus, functional monomer selection is a key point that can take advantage of the materials characteristics of MIPs that are not available to other binding/receptor systems.

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OP067
FATTY ACID ANALYSIS OF CORN SILK SAMPLES OBTAINED FROM TÜRKİYE

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Introduction: Zea mays L. (Poaceae) is an annual and monoecious plant. It is known usually maize or corn. The panicle male inflorescence is located on the upper part of the main stem, and the highly compressed spadix female inflorescence is located on branch apices emerging from the stem nodes (1). Corn silk (Maydis stigma) is used for medicinal purposes in many parts of the world. Traditionally, it has been employed as a diuretic and stone abortive in Türkiye (2). In this study, we aimed to analyze the fatty acid contents of corn silk samples purchased from various provinces of Türkiye in comparison with the standard sample.

Materials and Methods: 14 corn silk samples were obtained from eight different provinces of Türkiye. The following steps were performed in the fatty acid analysis protocol: sample preparation, total lipid extraction, methylation of fatty acids, and analysis of fatty acid methyl esters using GC-MS/FID techniques (3).

Results: Saturated fatty acids were determined to be dominant in the purchased samples, similar to the standard sample. The rate varied between 100% and 54.3%. Nonadecanoic acid, which is a saturated fatty acid, was determined as the major component in the whole corn silk samples. This component was followed by palmitic and linoleic acids, respectively.

Conclusions: It was determined that the analyzed samples were rich in saturated fatty acids, similar to the standard sample. Since corn silk samples are rich in saturated fatty acids, care should be taken when using them for human health, especially when prepared with a nonpolar solvent.

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OP068
IN VITRO PHOTODYNAMIC THERAPY EFFECTS OF SILICON (IV) PHTHALOCYANINE ON COLORECTAL CANCER CELLS

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Introduction: Colorectal cancer (CRC) ranks as the third most prevalent form of cancer globally (1). The treatment of CRC modalities include surgery, chemotherapy, radiotherapy, and immunotherapy. Nevertheless, these approaches frequently encounter constraints (2). The canonical Wnt pathway, is a signaling pathway that has been implicated in various biological processes such as cell proliferation and functional/structural cell differentiation (3). Photodynamic therapy (PDT), however, emerges as a minimally invasive treatment showing potential for enhancing CRC treatment efficacy. PDT entails administering a photosensitizer agent that selectively accumulates in cancer cells. Upon exposure to light at a specific wavelength, the photosensitizer activates, generating reactive oxygen species that induce localized cell death and tumor eradication (4, 5). In this study, we aimed to investigate the PDT effect of BD-SiPc against colorectal cancer cells (HCT-116) and its relationship with the canonical Wnt pathway, which plays a role in colorectal cancer pathophysiology.

Materials and Methods: The cytotoxic and phototoxic properties of BD-SiPc were assessed utilizing the MTT cell viability assay. To determine cell death mechanism on HCT-116 in the presence of BD-SiPc, annexin V/FITC apoptosis detection and mitochondria membrane potential assay were investigated using flow cytometer. Finally, western blotting (APC, p-GSK-3β, β-catenin, and caspase-3) analysis was performed to investigate the association with the PDT and Wnt signaling pathway.

Results: The findings revealed that BD-SiPc exhibited statistically significant phototoxic effect against HCT-116 cells compared to dark. Furthermore, BD-SiPc triggered apoptosis and disrupted mitochondrial integrity in HCT-116 cells under light irradiation. Western blot analysis indicated that expressions of APC and β-catenin significantly reduced on HCT-116 cells treated with BD-SiPc with light irradiation compared to the control group ($p<0.05$, $p<0.0001$). Additionally, the caspase-3 level was markedly elevated with BD-SiPc with light irradiation compared to the control group ($p<0.05$).

Conclusions: According to our results, BD-SiPc would be a promising candidate as a novel PDT agent for the treatment of colorectal cancer.

Acknowledgements: This work was supported by Office of Scientific Research Projects of Karadeniz Technical University. Project number: TSA-2022-9993

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OP069
TRYPTOPHAN METABOLISM, INFLAMMATION AND OXIDATIVE STRESS IN OSTEOARTHRITIS PATIENTS.

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Introduction: Osteoarthritis (OA) is a joint disease that is much more complex than a wear-and-tear disease and involves metabolic and biochemical mechanisms. Despite the high prevalence, there is currently no drug that can completely eliminate or repair the disease (1). Identification of biomarkers associated with OA may provide a better understanding of the underlying etiology and pathogenesis of this disease. The aim of our study is to examine the relationship of the tryptophan-kynurenine pathway with inflammation and oxidative stress in patients with OA.

Materials and Methods: A total of 78 participants, 52 patients and 26 controls, were included in the study. Tryptophan, Kynurenine, TNF-α, IL-36α, Neopterin, malondialdehyde (MDA), which is an oxidative stress marker, superoxide dismutase (SOD) and catalase (CAT) levels of the patient and control groups were measured. MDA level was measured spectrophotometrically according to the Ohkawa method. Catalase activity was determined according to the determination method determined by Aebi. The measurement principle of SOD enzyme activity was performed according to the Sun method. Tryptophan, Kynurenine, TNF-α, IL-36α, Neopterin levels were measured using BT-LAB brand commercial ELISA Kits.

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Results: The measured values were compared between the patient and control groups. The values of the patient group and the control group were SOD (10.79±3.6 U/L and 10.39±3.56 U/L), CAT (0,0182±0,0156 U/L and 0,0115±0,0162 U/L), MDA (5.89±0.83 mmol/L and 5.27±0.99 mmol/L), Kynurenine (86555.15±68721.75 ng/L and 107489.51±7729.,98 ng/L), Neopterin (43.57±57.85 ng/L and 37.84±44.65 ng/L), IL36α (0.2±0.22 ng/L and 0.15±0.03 ng/L), Tryptophan (20.21±14.64 ng/L and 22.61±10.4 ng/L), TNF α (43.77±184.13 ng/L and 95.21±440.82 ng/L), respectively.

Conclusions: Among these measured values, it can be seen that MDA values, IL-36α and Tryptophan values are statistically significant between the patient and control groups ($p < 0.05$). According to the study findings, it was concluded that determining IL-36α and Tryptophan parameters and using them as biomarkers in OA patients may be meaningful and valuable. However, larger patient-based research studies are needed to support the results obtained.

Acknowledgements: This study was supported by Mersin University Scientific Research Projects unit. Project Number: 2021-1-TP3-4231

OP070
A NOVEL ELECTROCHEMICAL SENSOR FOR THE DETECTION OF A TYROSINE KINASE INHIBITOR ANTICANCER DRUG

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Introduction: Nintedanib (NIN) is a tyrosine kinase inhibitor molecule effective in treating non-small-cell lung cancer (1). Electrochemical sensors are successfully applied for the detection of tyrosine kinase inhibitor drug molecules (2wherein β-CD served as the functional monomer, MTX as the template that was extracted afterwards, thereby creating the imprinted cavities complementary to the template in the polymer matrix. MTX could be specifically recognized and binding by the imprinted cavities. The developed MIP sensor exhibits a rapid electrochemical response, high sensitivity and selectivity for the determination of MTX in pharmaceutical formulations and spiked urine samples. Moreover, the proposed approach presents distinct advantages over reported electrochemical methods for determination of MTX because it is a one-step preparation and the template molecule could be easily removed by cyclic voltammetry scans, and no elution reagent is required. Under the optimal experimental conditions, the linear response range for MTX concentrations by the MIP sensor was 6 × 10−8 M–1 × 10−5 M with a detection limit of 3 × 10−8 M (S/N = 3). Even though, no electrochemical sensors are employed for NIN so far. Molecularly imprinted polymer (MIP) possess cavities complementary to the size and shape of the target analyte enabling their specific detection. To improve the sensitivity of MIP sensors, electrodes are modified with conducting materials. We aim to develop an efficient electrochemical sensor for the detection of NIN.

Materials and Methods: A bare GCE was modified with 5 µL of MWCNT and 2 µL of Rubbz by drop casting. The MIP layer was created on Rubbz/MWCNT/GCE via electropolymerization of o-PD in the presence of NIN. After polymerization, the template NIN was extracted from the MIP film by elution with ethanol at 250 rpm for 3 hours at room temperature. Following that the drug was rebound to the cavities by immersing the electrode in the drug solution for 5 min. The concentration of Nintedanib is determined by measuring the changes in charge transfer between MIP/Rubbz/MWCNT/GCE and the redox probe [Fe(CN)6]3-/4-.

Results: The analytical performance of the sensor was evaluated by the DPV technique. The calibration curve for NIN at different concentrations was linear in the range of 100-5000 pM. The LOD and LOQ values obtained were 18 pM and 56 pM respectively. Moreover, the applicability of the sensor was tested for spiked synthetic serum samples and the linear range was found to be 100-5000 pM. The LOD and LOQ values were 16.5 pM and 50 pM respectively. The sensor was also tested for Nintedanib content in Ofev® 150 mg capsule and successfully recovered 148.83 mg of the drug with a recovery percentage of 99.23%.

Conclusions: The results suggest that the sensor can be effectively used for the selective and sensitive determination of the Nintedanib drug.

Acknowledgments: This study was supported by a grant from the Türkiye Bursları Research Scholarships Program numbered 23IN003709

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OP071
POLY(3,4-ETHYLENEDIOXYTHIOPHENE) NANOWIRE-COATED PENCIL GRAPHITE ELECTRODE FOR ELECTROCHEMICAL DETERMINATION OF 5-FLUOROURACIL

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Introduction: 5-FU is a form of uracil in which a fluorine atom has replaced the hydrogen atom at the C-5 position and has been used since 1957, particularly in the treatment of colorectal and breast cancer. The optimum concentration of 5-FU in biological fluids should be monitored since different 5-FU metabolites affect RNA formation and thymidylate synthase (TS) activity. Moreover, the overdose of 5-FU causes side effects such as paralysis, diarrhea, and gastrointestinal mucositis, and therefore, its determination is significant (1). Poly(3,4-ethylenedioxythiophene) (PEDOT), one of the conducting polymers, shows long-term electrochemical stability and electroactivity in phosphate buffer solution (PBS) pH 7 (2). In this study, poly(3,4-ethylenedioxythiophene) nanowires (PEDOT NWs) were electrochemically synthesized on the surface of a pencil graphite electrode (PGE) and used for the electrochemical detection of 5-FU for the first time.

Materials and Methods: Electrochemical characterization of the designed electrode was realized using cyclic voltammetry (CV) and electrochemical impedance spectroscopy (EIS). pH optimization, calibration study, repeatability, reproducibility, interference, stability, and sample studies with PEDOT NW modified PGE were carried out using the DPV method. The surface images of the PEDOT NWs modified PGE were recorded with field emission scanning electron microscopy (FESEM). The structural characterization of the PEDOT was performed by Fourier transform infrared (FT-IR) spectroscopy. PEDOT NWs modified PGE was used to develop recovery studies for three different concentrations selected within the calibration range in the pharmaceutical 5-FU injection sample.

Results: The oxidation peak currents were studied at different pH levels in the PBS, and the optimum pH was found to be 7. The PEDOT NWs modified PGE displayed a 4-100 µmol L–1 linear range and 0.80 µmol L–1 limit of detection (LOD) for the determination of 5-FU. The developed method has advantages such as simple operation, short time, and low cost.

Conclusions: The designed PGE showed high selectivity, sensitivity, repeatability, reproducibility, and stability for detecting 5-FU.

Acknowledgments: We thank Deva Holding for providing this pharmaceutical active substance.

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OP072
A NOVEL STABILITY-INDICATING HPLC METHOD FOR DETERMINATION OF VORAPAXAR AND HIGH-RESOLUTION MASS SPECTROMETRIC CHARACTERIZATION AND MOLECULAR DOCKING STUDIES ON ITS NOVEL DEGRADATION PRODUCT

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Introduction: Vorapaxar (VOR) was developed as a protease-activated receptor-1 (PAR1) inhibitor for patients with established cardiovascular diseases (1). The objective of this study was to develop a validated stability-indicating HPLC method for analysis of VOR in pharmaceuticals; in addition, characterization of a novel degradation product (DP) with MSn studies and clarify its formation mechanism was realized within this context.

Materials and Methods: A reversed phase HPLC method was optimized to accomplish specific detection of VOR in the presence of its DP. The degradation studies were performed by applying different stress conditions on VOR, including heat, acid, alkali, oxidative, etc., and analyzing the resulting solutions using LCMS-IT-TOF instrument. Analytical method validation was performed according to the ICH Q2(R2) guideline. Molecular docking studies on the DP was evaluated using Molecular Operating Environment (MOE, 2019.0102) software, the protein structure of PAR1 bound with antagonist VOR (PDB ID: 3vw7, resolution 2.2 Å) was obtained from the RCSB Protein Data Bank. The physicochemical and pharmacokinetic parameters of the DP were predicted using the freely accessible in silico SwissADME web tool (http://www.swissadme.ch).

Results: The calibration curve was within the range of 0.3-12.0 µg/mL, and the LOD and LOQ were 0.05 and 0.15 µg/mL, respectively. Inter-day and intra-day precision were also assessed, and an RSD% under 2 was observed; accuracy was between 95% to 102%. In the stability experiments, formation of a novel DP, with an estimated mass of 510.66 g/mol, was observed under basic conditions. It is predicted that the degradation product is formed by breaking a double bond between atoms 9-10 in the VOR molecule and introducing the hydroxyl group into site 9.

Conclusions: A new HPLC method was successfully developed and validated for quantitation of VOR. In addition, a novel DP was characterized, and its activity and toxicity were assessed through molecular docking studies. Although DP doesn't show serious toxic effects, it is suggested that it interacts in different way than VOR with other cytochromes. The method possesses sufficient sensitivity for quantitative determination of the VOR in pharmaceutical preparations.

Acknowledgments: This study was supported by a grant from the Anadolu University Scientific Research Projects Commission (Project ID: TDK-2024-2442).

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OP073
ASSESSMENT OF NEURTURIN RS546726197 AND RS1260331466 SNPS IN BREAST CANCER RISK

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Introduction: Neurturin (NRTN) is a member of the GDNF family of ligands, a subclass of neurotrophic factors, and the protein complex formed by the binding of NRTN to its coreceptor GFRα2 activates the transmembrane receptors RET. NRTN, promotes cell survival, proliferation, differentiation, migration, and oncogenic effects by activating several signal transduction pathways through RET. Because activation of RET requires interaction with NRTN, genes encoding NRTN are thought to play a role in the pathogenesis of various types of cancer (1). The current study aimed to investigate the association between breast cancer risk and Neurturin polymorphisms.

Materials and Methods: The study group consisted of those who applied to Gazi University Medical Faculty Hospital and Dr. Abdurrahman Yurtaslan Oncology Training and Research Hospital General Surgery Outpatient Clinics it consists of 102 patients diagnosed with breast cancer and 102 healthy women. NRTN gene rs546726197 and rs1260331466 SNPs were investigated by the Sanger sequencing method in blood samples taken from the study group into K3EDTA tubes.

Results: In the Neurturin gene variants heterozygote/homozygote+wild genotypes distributions were found for rs546726197 (2/100) and rs1260331466 (5/96) in breast cancer patients. No significant association was found between both rs546726197 and rs1260331466 polymorphisms and breast cancer risk in terms of genotype distributions ($p>0.05$, $p>0.05$, respectively).

Conclusions: In breast cancer, which is the most common type of cancer in women, elucidating the genetic factors underlying the pathology and choosing the appropriate treatment is of great importance. Activation of RET via GFL, which involves NRTN and promotes tumor growth and spread, is a much-investigated pathway today. There are two studies on other polymorphisms in the NRTN gene, one in Hirschsprung disease and one in medullary thyroid carcinoma, however, there is no data in the literature about the rs546726197 and rs1260331466 variants (2, 3). Our study will contribute to the literature with new results and shed light on future studies.

Acknowledgement: None

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OP074
ESTABLISHMENT OF 3D INFLAMMATORY MICROENVIRONMENT MODEL OF PROSTATE CANCER IN DRUG DEVELOPMENT STUDIES.

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Introduction: Molecular changes in the inflammatory prostate microenvironment lead to PCa by triggering epithelial-mesenchymal transition (EMT), which plays an important role in cancer initiation and metastasis. However, reliable, accessible, and applicable in vitro cancer models are required for both the investigation of the cellular mechanisms of cancer development and the analysis of accurate drug efficacy in anticancer drug research. In recent years, 3-dimensional (3D) spheroid and organoid models in cell culture have been developed to better model many types of cancer, including PCa. Recent literature shows that 3D cell culture is more successful in representing cell-cell interactions and cellular drug response than 2D. Therefore, we established an in vitro 3D inflammatory microenvironment model of PCa for further use in anticancer drug development studies. Alterations in EMT markers and the role of NKX3.1, a tumor suppressor in PCa, were determined and analyzed in 2D and 3D cell culture models in comparison. ,.(1–5)

Materials and Methods: To create prostate spheroids, cells were seeded on poly-HEMA coated U bottom plates and centrifuged at 200g for 10 min. After determining the optimal cell number for the spheroids of RWPE1 prostate epithelial cells, LNCaP, DU145, and PC3 prostate cancer cell lines, the spheroids were treated with a conditional inflammatory medium. Cell viability of spheroids in 3D cell culture was analyzed by 3D cell titer-GLO and compared with cell viability of 2D cell culture. Alterations in EMT markers in 2D and 3D cell culture models were detected by immunoblotting w/w.o. NKX3.1 overexpression in PCa cell lines.

Results: The effect of the inflammatory conditioned medium on cell viability was compared in 2D and 3D cell culture models. Significant differences in protein levels of NKX3.1, Fibronectin, E-cadherin, Vimentin, Snail-1, and Twist-1 were detected in 2D and 3D prostate cancer models of androgen-responsive LNCaPs and castration-resistant DU145 and PC3s. The increase in fibronectin levels upon inflammation was higher in spheroids and ectopic expression of NKX3.1 enhanced the increase in castration-resistant cells. E-cadherin, vimentin, and Twist-1 were shown to be increased in 3D spheroids. These results suggested that 3D spheroid models exhibit different results from 2D in EMT transition model of PCa.

Conclusions: A 3D cell culture model was established to mimic the inflammatory microenvironment in PCa cell lines and 3D cell culture model was shown to better mimic inflammation-induced EMT transition in PCa suggesting the use of this model is crucial in drug development studies.

Acknowledgements: This study was supported by a grant from TUBITAK (222S863) and Ege University (27410)

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OP075
INVESTIGATION OF THE MECHANISM OF PLATELET INHIBITOR CANDIDATES WITH ANTIPLATELET EFFECTS.

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Introduction: Platelet aggregation, which causes a plug, is a life-threatening factor for people worldwide. Antiplatelet drugs used in the clinic prevent thrombosis but also have some disadvantages, such as increasing the risk of bleeding. Therefore, new research is still ongoing to prevent platelet activation and aggregation in order to reduce mortality and prevent thrombosis. Glycoprotein VI (GPVI), which is the main receptor of collagen, has shone in the field of new safe targets. However, the drug as a GPVI antagonist has not still been discovered and there isn't on the market (1).

Materials and Methods: To discover novel platelet antagonists, five compounds were selected from the Chemspace chemical database. The filter was made by chemical similarity screening in silico, based on the Tanimoto coefficient. For the selected compounds' antiplatelet activities in vitro, the receptor selectivity and specificity were evaluated by generating platelet aggregation induced by platelet receptor agonists; GPVI agonists (collagen; 3 µg/ml, convulxin; 100 ng/ml), the CLEC-2 agonist (rhodocytin; 1 µg/ml), and the potent platelet agonist thrombin (0.1 U/ml) in washed platelets (2x108 platelets/ml).

Results: Our biological activity results showed all compounds exhibited very strong inhibition against platelet aggregation. The IC50 values of all compounds were found below 5 µM.

Conclusions: Compound 22 (Figure 1) was found to be the most active compound (IC50 value of 1.54 µM for collagen and 1.11 µM for rhodocytin), and compound 19 was found to be the most specific to the GPVI receptor compared to the other compounds (IC50 value of 1.53 µM for collagen and 3.52 µM for rhodocytin). These data provide guidance for the design of new therapeutic platelet antagonist candidates.

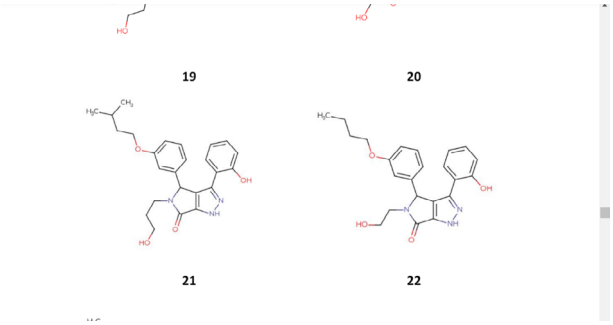

Figure 1. Chemical structure of the most active compound 22.

Acknowledgements: This study was supported by a grant of TUBITAK (SBAG-222S662).

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OP076
DELIVERY OF MIR-21I/PTX BY GLYCOPEPTIDE NANOPLEXES FOR THE ANTICANCER TREATMENT OF MELANOMA

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Introduction: Melanoma is the leading cause of death from skin cancer and traditional treatments for melanoma have not proven highly effective and show severe side effects (1,2). Advancements in technology are enabling further research into combination treatments, such as photodynamic therapy offering new hope for treating cancers (3). RNA interference, a process of post-transcriptional gene silencing with small molecules like miRNAs can effectively block the expression of specific genes and their combination with other therapies has been shown to enhance the antitumor response. Delivery system-based phototherapies are widely used for cancer treatments (4). Aim of this study is to create nanoplexes with miR-21i able to inhibit tumor progression and overcome paclitaxel resistance in melanoma.

Materials and Methods: In this study, biomimetically constructed cationic glycopeptide nanocarrier systems were created by condensing sugar and peptide monomers. These glycopeptide polymers were linked with protoporphyrin IX and micellar formulations were developed by encapsulating paclitaxel (PTX) and incorporating miR-21i into the nanocarrier system to effectively target melanoma cells. This delivery system was examined with in vitro tests such as cell viability, migration and invasion, apoptosis, cell cycle and ROS production capacity analysis using melanoma and normal skin cell line.

Results: Combined therapeutic efficacy for PTX/miR-21i demonstrated significant decrease in viability for melanoma cell line and showed effective intracytoplasmic release due to its pH-triggered sequential degradation within tumor cells. Nanocarrier system carrying PTX and miRNA21 was observed to increase apoptosis and reduce the migration of cells in the melanoma cell line.

Conclusions: In vitro tests indicated that this phototherapeutic nanocarrier system provided excellent synergistic therapeutic effects against melanoma. This PS-based cationic glycopeptide nanoplatform holds promise for the co-delivery of drugs and genes in treating various cancers.

Acknowledgements: This study was supported by the Scientific and Technological Research Council of Türkiye (TUBITAK, Project No: 122Z731).

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OP077
THE SYNTHETIC CANNABINOIDS CP55-940 AND WIN 55212-2 INDUCED IRON DYSREGULATION AND OXIDATIVE STRESS IN HUMAN GLIOBLASTOMA CELLS.

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Introduction: Glioblastoma is an aggressive tumor of the central nervous system (CNS). The lack of effective treatment options, and therefore low survival rates, constitutes an urgent requirement for the development of new approaches in therapy (1). CP55-940 (CP) and WIN 55212-2 (WIN) are synthetic cannabinoids that act as cannabinoid receptor-1 (CB1) agonists. They have been reported to exert both neuroprotective and anticancer activities (2). However, their potential role in cellular iron metabolism have not been unveiled so far. In the present study, we evaluated the effect of CP and WIN in glioblastoma cell lines.

Materials and Methods: The effect of CP and WIN on U118MG human glioblastoma and L929 healthy cells were assessed by the MTT assay. Oxidative stress was detected with DCFHDA staining. The state of intracellular iron and lipid was evaluated with modified Perls and Sudan III staining under light microscope, respectively. Furthermore, the potential interaction of labile iron with lipids in the presence or absence of iron modulators (ferric ammonium citrate, deferoxamine) and scavengers (n-acetylcysteine, mannitol), were investigated by co-localization experiments using confocal microscopy.

Results: The cytotoxic effect of CP (16 µM) and WIN (8 µM) at 24 h in U118MG cells was determined as 56,03±1,18 and 52,83±1,81 (%), whereas in L929 cells, the viable cell rates were detected as 79,79±4,39 and 63,89±2,00 (%), respectively. According to further viability assays, the cytotoxic activity of CP and WIN started at 6 h. While the effect of WIN gradually decreased over 24 h, the toxicity of CP remained stable for 12 h and then exhibited similar pattern with WIN. Further experiments revealed increased oxidative stress as well as detectable iron and lipid co-localization which was predominantly inhibited by deferoxamine (250 µM) and mannitol (25 mM) following 6 h of treatment with CP and WIN.

Conclusions: In conclusion, the findings of the present study demonstrated for the first time that CP and WIN altered cellular iron metabolism and increased oxidative stress in human glioblastoma cells, indicating the iron modulatory effects of cannabinoids and therefore the potential contribution in the treatment.

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OP078
IODINATED SI-FLUORESCEIN BASED PHOTOSENSITIZER AS A THERANOSTIC AGENT AGAINST HUMAN GLIOBLASTOMA CELLS.

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Introduction: Glioblastoma (GBM), which is a highly aggressive and lethal type of glioma, remains a significant challenge in modern medicine. Photodynamic therapy (PDT) is an emerging light-based alternative approach with several advantages, including high efficiency, minimal invasiveness, and a lack of side effects compared to traditional treatments like chemotherapy and radiotherapy. In PDT applications, fluorescein-based photosensitizers are commonly used due to their water solubility, photostability, and ease of modification for improvement towards the near-infrared region with enhanced photochemical properties for deep tissue applications. β-galactosidase (β-gal) is a popular biomarker overexpressed in several cancer types, including gliomas. Herein, we investigated β-gal activatable Si-fluorescein-based phototheronastic agent for treating brain cancer.

Materials and Methods: Human glioblastoma (U87MG) and mouse fibroblast (L929) cells were used to test an enzyme-activating PDT agent, β-Gal-SiF-II. To determine toxicity of β-Gal-SiF-II, both U87MG and L929 cells were treated with β-Gal-SiF-II (0 -10 μM) for 24 hours (dark) or 1 h followed by illumination at 595 nm (9.38 mW/cm², 2 h). MTT analysis was held either with or without scavengers of: N-acetylcysteine, mannitol, trolox or sodium azide. DCFDA, AO/EtBr staining and subcellular localization assays were performed with confocal microscopy.

Results: Our findings indicated that β-Gal-SiF-II reduced cell viability of U87MG (IC50: 3.301μM) significantly whereas it showed less cytotoxicity in L929 healthy cells (IC50: 6.270μM) under light irradiation. Mitochondrial and lysosomal localization of activated β-Gal-SiF-II led to elevated ROS generation and apoptotic cell death which was confirmed by DCFDA and AO/EtBr staining, respectively.

Conclusions: The enzyme-activating PDT agent, β-Gal-SiF-II, has the potential to advance brain cancer treatment and diagnostics.

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OP079
MULTIPLE BIOLOGICAL APPROACH TO INVESTIGATE THE EFFECS OF SILENE VULGARIS (MOENCH) GARCKE

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Introduction: The Silene genus is the largest member of the Caryophyllaceae family and is represented by more than 700 species. 59 of the 141 species growing in Türkiye are endemic (1). Silene species are consumed as food, and it is traditionally used in the treatment of respiratory, gastrointestinal and urinary tract disorders, cuts and inflamed wounds (2). This genus, Silene, contains various secondary metabolite groups such as flavonoids, anthocyanins, terpenes, triterpenes, triterpene glycosides, steroid derivatives and saponins. (1). There are studies on the antioxidant, antimicrobial, antiinflammatory, antitumor, immunomodulator, adaptogen, hepatoprotective and insecticidal effects of extracts and pure compounds obtained from Silene species in the literature (3). In this study, we aimed to determine multiple biological effects of various extracts of Silene vulgaris which was collected from Trabzon Çaykara Soğanlı Village on May 2022.

Materials and Methods: The pure methanol extract (SM) was dissolved in distilled water and its chlorophylls were removed with n-hexane (2). Then its subfractions were obtained named n-butanol, chloroform and water for biological acitivity tests. Total phenolic/flavonoid content, antioxidant (DPPH and FRAP), tyrosinase and α-glucosidase inhibitory effects of the extracts were evaluated using spectrophotometric methods. In addition DNA and BSA damage protective effects of the extracts against Fenton reagents were investigated using agarose and SDS-PAGE gel electrophoretic methods (4).

Results: The results showed that n-butanol extract has the highest total phenolic and flavonoid contents with 166.00 ± 4.36 mg GAE/g dry weight and 144.16 ± 8.55 mg QE/g dry weight. Consistent with these results, while n-butanol extract showed concentration-dependent DPPH radical scavenging activity, it also has the highest result in FRAP activity (495.40 ± 3.94 mM BHAE/ g dry weight). Tyrosinase and α-glucosidase inhibition activities of all extracts showed lower effects than positive controls. In electrophoretic studies, while no damage was observed on DNA and BSA at the studied concentrations of n-butanol extract, it was determined that it had a strong protective effect against DNA and BSA damage caused by Fenton reagent.

Conclusions: These findings revealed n-butanol extract has the potential to be used in many diseases due to its rich in antioxidant and protective effects.

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OP080
EPIDERMAL ALTERATIONS IN HUMAN KERATINOCYTE CELLS INDUCED BY DERMAL THIRDHAND SMOKE EXPOSURE

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Introduction: Thirdhand smoke (THS) is residual cigarette smoke that settles on indoor surfaces, fabrics, and dust, accumulating in the environment. As a result, it may pose a risk for individuals who come into frequent contact with THS-contaminated surfaces. The present research aims to investigate the toxicity of dermal THS exposure in HaCaT human keratinocytes via oxidative, inflammatory and matrix metalloproteinase (MMP) level alterations.

Materials and Methods: The THS was extracted from terrycloth exposed to 3R4F research cigarette smoke in a closed chamber. Mitochondrial and lysosomal cell viability, intracellular GSH level, total SOD activity, MMP-1 and IL-6 levels were detected as similar in our previous study (1). The diminished cell migration capacity of THS-exposed cells was assessed via scratch assay. Sulforaphane (SFN), a potent antioxidant isothiocyanate compound was used as a negative control.

Results: THS had a dose-dependent cytotoxic effect (12.5%-100%, v/v) on HaCaT cells due to mitochondrial cell dysfunction ($p < 0.01$), which was mitigated by SFN (0.62 µM) treatment. THS exposure also lowered intracellular GSH accumulation and T-SOD activity in keratinocytes. Increased MMP-1 expression in THS-exposed cells led to collagen breakdown, delayed wound healing, and increased pro-inflammatory response in a dose-dependent manner ($p<0.05$). The findings are likely to raise awareness about THS as an environmental hazard for the skin, particularly in populations with the highest cigarette consumption rates.

Conclusions: To summarize, our findings may contribute to research on the role of dermal exposure to THS in the development of epidermal changes and other skin diseases.

Acknowledgements: This study was financially supported by TUBITAK 2209A—a research support program for undergraduate students.

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OP081
PERCEPTIONS OF THIRDHAND SMOKE AND NOVEL TOBACCO PRODUCTS OF A COLLEGE IN TURKEY

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Introduction: Turkey is one of the highest top-ranked countries for smoking rate, among the OECD countries. Hence, as a newly emerging environmental health concern, thirdhand smoke (THS), has a greater impact on public health by resulting in residual smoke accumulation as well as leading to a deposition of toxins from secondhand smoke (SHS) in the environment (1). This study aims to evaluate the smoking habits, awareness of the THS concept, and new generation tobacco products (NGTP) use of Acibadem Mehmet Ali Aydinlar University campus, a health-science-based college in Turkey, to develop safer and sustainable campus strategies.

Materials and Methods: The evaluation was performed via an online survey that was applied to university students, and academic and administrative staff at Acibadem Mehmet Ali Aydinlar University between March and May 2023 voluntarily through online platforms. The questions were designed to measure lifestyle and social factors such as demographic characteristics, smoking levels, general information about e-cigarettes and NGTPs, social approaches to environmental cigarette smoke (CS), and THS awareness, as well as to clarify campus recognition according to the methods of Haardörfer et al. (2017) and Cadirci et al. (2021) (2,3).

Results: Based on research findings, 46.0% (n=177) of the participants were smokers, and 54.0% (n=208) were non-smokers. Most participants, unfortunately, had never heard the name of THS (73.8%), but were aware of the possible public health hazards with a moderate BATHS score, 35.97 ± 7.38. Surprisingly, there is not a distinct difference in the knowledge of e-cigarette content as well as the NGTP concept among students.

Conclusions: Even though passive and active smoking is well known by people, it is crucial to emphasize the concept of THS to inform people in the fight against tobacco. Our results showed that participants had a noticeable lack of knowledge about THS, e-cigarettes and NGTP and further studies on these topics are needed for smoke-free campuses and stronger anti-smoking policies.

Acknowledgements: None

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OP082
INVESTIGATING THE IMPACT OF ALUMINUM HYDROXIDE ON DIFFERENTIATION PATHWAY IN SH-SY5Y CELL LINE

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Introduction: Aluminum (Al), the third most prevalent element in the earth's crust, has long been implicated as a potential contributor to Alzheimer's disease (AD). Aluminum can cause the accumulation of deposits in organs, leading to tissue anomalies and numerous harmful effects in both experimental animals and humans. Elevated concentrations of Al are associated with an increased susceptibility to several neurodegenerative conditions, which has sparked interest in understanding its role in the human body and the intricate mechanisms underlying Al-induced neurotoxicity1,2. This study aims to uncover the neurotoxic effects of aluminum in an Alzheimer's disease-like in vitro model by examining its impact on neuronal function and viability within a cell culture setting, focusing on key pathways associated with AD pathology.

Material and Methods: SH-SY5Y cells were initially cultured in a standard growth medium and then induced to differentiate by reducing fetal bovine serum concentration and introducing retinoic acid (RA) into the culture medium. Brain-derived neurotrophic factor was subsequently added with RA, and the differentiation process was completed by the seventh day. The study comprised four groups: control, Al-exposed, AD model, and AD model with Al exposure. The groups were exposed to 362 µM aluminum for 7 days. Hyperphosphorylated tau protein, a specific marker of AD, was quantified in all groups. Additionally, the comparative analysis included the glycogen synthase kinase-3 (GSK-3) β, protein phosphatase 2A (PP2A), human serine/threonine-protein phosphatase PP1-alpha catalytic subunit (PPP1CA), Akt, and Wnt signaling pathways. Oxidative stress parameters (total antioxidant capacity, lipid peroxidation, protein carbonyl, and reactive oxygen species) were also evaluated across the study groups.

Results: Our study investigates the effects of aluminum on GSK-3β and the Wnt/β-catenin pathways, alongside an array of oxidative stress parameters. Notably, aluminum exposure precipitates a surge in GSK-3β levels while concurrently dampening PP2A and Akt activity, culminating in an escalation of tau levels within the cellular milieu. Furthermore, aluminum appears to impede the Wnt pathway. Aluminum exposure also elicits an increase in cellular reactive oxygen species levels, along with elevated levels of malondialdehyde, protein carbonyls, and glutathione, indicative of compromised antioxidant systems.

Conclusions: These findings provide valuable groundwork for understanding the potential role of aluminum in promoting neurodegeneration in AD. They pave the way for further research into strategies aimed at protecting against aluminum-induced toxicity in neurological contexts.

Acknowledgement: The project was partially supported by the Hacettepe University Scientific Research Projects Fund (Project No: TSA-2021-14186).

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OP083
THE INVESTIGATION OF TOXICITY OF FLAME RETARDANT ADDITIVES FOR PLASTICS BY USING IN SILICO METHODS

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Introduction: Plastics which are utilized in everyday life for medical treatments and technological developments, make polymers more flexible. Flame retardant additives are using in plastics for fireproof feature. Flame retardant additives for plastics may be present in a variety of environmental elements, such as food, drink water, wastewater, dust, and air. (1) They are involved into a large group chemicals, in our study we selected 5 compounds: tris(2- chloroethyl) phosphate (TCEP), tris(1,3-dichloro-2-propyl) phosphate (TDCPP), triphenyl phosphate (TPHP), tri-o-cresyl phosphate (tri-o-tolyl phosphate) (ToCP), tris(1,3-dichloro-2-propyl) phosphate (TDCIPP), and triethyl phosphate (TEP) that are frequently used as on the plastic products. In this study; the carcinogenic, mutagenic, endocrine disrupter and mitochondrial toxicity potencies of 5 different compounds of the OPFRs investigated by using a computational toxicology method: ProTox-II and we aimed to assess the precision and dependability of the in silico predictions.

Materials and Methods: The goal of this validation research was to evaluate the prognostic accuracy of the cheminformatics-based in silico model, ProTox-II, in predicting the toxicity of common plasticizer chemicals present in a range of goods. With its integration of machine learning models grounded on cheminformatics principles, the ProTox-II platform provides a complete method for predicting toxicity.

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Results: Acute toxic effects were predicted from the Lethal Dose 50 (LD50) values; TCEP classified in Group 4 that means "Slightly toxic" and it was found to be active in terms of carcinogenic effects. TDCPP classified in Group 4 that means "Slightly toxic" and it was found to be active in terms of carcinogenic effects, mutagenicity and aromatase enzyme activity. TPHP classified in Group 4 that means "Slightly toxic" and it was was found to be active in terms of AhR Activity, Estrogen Receptor Alpha (ERα) Activity and Mitochondrial Membrane Potential (MMP). ToCP classified in Group 4 that means "Slightly toxic" and it was found to be active in terms of AhR Activity and MMP. TEP classified in Group 4 that means "Slightly toxic" and it was found to be active in terms of carcinogenicity and AhR Activity.

Conclusion: In conclusion, this study used the in silico ProTox-II approach to examine the mutagenic, carcinogenic, endocrine disruptor, and mitochondrial toxicity potencies of selected compounds. This study offered fresh perspectives on the potentially harmful consequences however, further research is required to assess their toxicitythese results establish the foundation for the studies on toxicity both in vivo and in vitro.

Acknowledgements : No funding to declare

OP084

IDENTIFICATION AND COMPARISON OF MET RECEPTOR TYROSINE KINASE GENETIC DIFFERENCE (RS1858830) IN HEALTHY CONTROL AND AUTISM SPECTRUM DISORDER CASES.

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Introduction: Autism spectrum disorder (ASD) is a developmental disease marked by limited, repetitive behavioral patterns as well as difficulties with social interactions and communication [1]. Genome-wide studies have attempted to identify potential regions that may have role, MET receptor tyrosine kinase (MET) gene rs1858830 has been linked with a signal in ASD [2]Vanderbilt University, Nashville, Tennessee 37232, USA. daniel.campbell@vanderbilt.edu</auth-address><titles><title>Genetic evidence implicating multiple genes in the MET receptor tyrosine kinase pathway in autism spectrum disorder</title><secondary-title>Autism Res</secondary-title></titles><periodical><full-title>Autism Res</full-title></periodical><pages>159-68</pages><volume>1</volume><number>3</number><edition>2009/04/11</edition><keywords><keyword>Alleles</keyword><keyword>Autistic Disorder/*genetics</keyword><keyword>Exons/genetics</keyword><keyword>Genotype</keyword><keyword>Hepatocyte Growth Factor/genetics</keyword><keyword>Humans</keyword><keyword>Linkage Disequilibrium</keyword><keyword>Plasminogen Activator Inhibitor 1/genetics</keyword><keyword>Proto-Oncogene Proteins/*genetics</keyword><keyword>Proto-Oncogene Proteins c-met</keyword><keyword>Receptors, Growth Factor/*genetics</keyword><keyword>Receptors, Urokinase Plasminogen Activator/genetics</keyword><keyword>Signal Transduction/physiology</keyword></keywords><dates><year>2008</year><pub-dates><date>Jun</date></pub-dates></dates><isbn>1939-3806 (Electronic. The aim of the current study is the identification of (MET) gene rs1858830 genotype and presentation of genotype& allele frequencies in ASD patients and healthy controls.

Materials and Methods: The study was conducted on patients consulted at Ankara University School of Medicine, Department of Psychiatry. Blood samples were collected, and genomic DNA was isolated by use of the high salt method. Genetic identification of the MET gene (rs1858830, C>G) was conducted using polymerase chain reaction–restriction fragment length polymorphism method.

Results: A total of the 41 cases, 20 (48.78% of patients) were healthy control, whereas 21 (51.22% of them) were ASD patients. The mean age was (33.00±9.68) for the ASD population whereas it was (30,30±10.19) for the healthy controls. The genotype frequencies were 38.09, 28.57 and 33.33 for CC, CG and GG genotypes and 30.00, 50.00 and 20.00 for ASD and control cases respectively. Allele frequencies were 52.38, 47.62 for ASD and 55.00 and 45.00 for controls regarding C and G alleles respectively. Both samples were found to be in equilibrium for Hardy-Weinberg (control: X2=0.02, p=0.96, and ASD: X2=3.93, p=0.05, df=1).

Conclusions: The identification of rs1858830 genotype and allele frequencies in the Turkish population with ASD & control cases holds critical importance by advancing our understanding of the genetic basis of the disorder, facilitating personalized approaches to treatment, and for early detection.

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OP085
MOLECULAR EFFECTS OF ABEMACICLIB ON KERATINOCYTE CELLS

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Introduction: Abemaciclib, a cyclin-dependent kinase inhibitor, was approved by the Food and Drug Administration in 2017 for use as a monotherapy or in combination with aromatase inhibitors/endocrine therapy for the treatment of breast cancer (1). Alopecia and pruritus are common dermal reactions due to abemaciclib use (2). In recent years, it has also been reported that abemaciclib induced some cutaneous reactions including Henoch-schönlein purpura, hyperpigmentation and radiation recall dermatitis (3,4). The mechanisms of cutenous dermal reactions caused by abemaciclib has not been known yet. Therefore, it was aimed to investigate the molecular effects of abemaciclib on keratinocyte cells in the study.

Materials and Methods: The cytotoxic effects of abemaciclib on keratinocytes (HaCat cell line) were examined using MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) and lactate dehydrogenase (LDH) release assays following 24 h exposure. The production level of reactive oxygen species (ROS) was evaluated by H2DCFDA (2′,7′-dichlorodihydrofluorescein diacetate) staining, apoptotic/necrotic cell death was investigated using Annexin V/Propidium iodide staining and the results were analyzed through flow cytometry. Tumor necrosis factor alpha (TNF-α) secretion was evaluated by Legendplex assay using flow cytometry.

Results: Abemaciclib have shown a dose-dependent effect on cell viability. The half maximal inhibitory concentration (IC50) value was determined as 24.18 µM and 30.87 µM according to the MTT and LDH assays, respectively. ROS production and apoptotic cell death were increased after abemaciclib treatment. TNF-α secretion was induced following abemaciclib treatment.

Conclusions: The preliminary study showed that oxidative stress and inflammatory response may be responsible for abemaciclib-induced cutenous reactions. However, further studies are needed to confirm our findings.

Acknowledgements: This study was supported by a grant of TUBITAK (SBAG-223S827)

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OP086
DEVELOPMENT AND CHARACTERIZATION OF IVERMECTIN LOADED MICRONEEDLE FORMULATIONS USING 3D PRINTED MOLDS

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Introduction : Ivermectin is a broad-spectrum antiparasitic semi-synthetic drug and has low solubility in water (1). The main goal of the fabrication of microneedles is to achieve easy penetration to skin for enhancing drug permeability. However, fabrication of microneedles is very challenging mainly due to the three-dimensional (3D) conical geometry in micron scales (2). In our study, we aimed to develop low-cost microneedle formulations with high standardization.

Materials and Methods : The main mold, which was printed with an SLA type 3D printer, was matched with a platinum-based curable polydimethyl siloxane (PDMS), and then microneedle mold was created.

Ivermectin (3.3 mg), methanol, PEG 400 and water were mixed in a beaker to obtain a homogeneous mixture contains the amounts in Table 1. 0.6 g of the mixture was weighed and placed in silicone molds. It was kept under laminar flow for 48 hours to dry. Than polymeric microneedles were peeled from mold.

To evaluate the mechanical strength of microneedles, the vertical stiffness value (N) per needle was determined. In in vitro drug release study, microneedle formulations were placed in beakers in a pH 7.4 buffer environment containing 1% Tween 80, and ivermectin release was examined at 37°C under constant stirring and analyzed using validated HPLC method.

In order to determine the skin penetration properties of microneedles were also evaluated in vitro and ex vivo penetration studies using fluorescence and scanning electron microscopy.

Table 1: Candidate Microneedle Formulations and Mechanical Properties (n=10, mean±SD)

Formulation content PVP K90: PVP K30 (g)	PEG 400 (g)	Methanol (g)	Water (g)	N (N/cm^2)	Mean Needle Tip Diameter (µm)	Mean Needle Height (µm)	Mean Base Diameter (µm)
F1 (1:3)	0.4	7.8	7.8	6.00	101±20	451±18	278±25
F2 (2:2)	0.4	7.8	7.8	7.06	98±16	439±23	264±28
F3 (3:1)	0.4	7.8	7.8	12.84	87±13	420±24	250±24
F4 (2:0)	0.4	8.8	8.8	2.87	73±10	439±20	226±9

Results: Considering the needle tip and base sizes, the most suitable formulations were determined as F3 and F4 (needle tips 87±13 and 73±10 respectively), however durability of F4 was insufficient (N=2.87 N/cm2). Approximately 85% release amount of ivermectin was obtained for all formulations within 30 minutes. It was observed that F1 and F3 could penetrate appx. 381 µm. In SEM images of ex vivo penetrated skin samples, the holes that created by F1 and F3 were found to be deeper.

Conclusions: F1 and F3 were selected for use in future studies due to their more suitable mechanical, penetration and release properties. As a result, we have produced highly standardized microneedles suitable for the use of ivermectin in various dermal diseases.

Acknowledgements: This study was supported by Gazi University Scientific Research Projects Coordination Unit under grant number TSG-2022-7934. Ivermectin was generously gifted by Zoeticals LLC.

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OP087
IN VITRO EVALUATION OF INSULIN LOADED-3D PRINTED WOUND DRESSING

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Introduction: Insulin is a hormone that regulates blood sugar, but in recent years its use in wound healing has attracted attention because it enables the reconstruction of damaged skin. (1). The aim of this study is to develop and evaluate 3D printed insulin loaded sodium alginate (SA)-silk fibroin(SF) based wound dressings.

Materials and Methods: Silk fibroin was produced from Bombyx mori cocoons (2). Ink formulations were prepared with mixtures of 5% and 7.5% concentrations of sodium alginate and 5% silk fibroin solutions in different ratios. (Figure 1a). Viscosity, rheological properties, and printability of inks were evaluated. Insulin loaded wound dressing was printed using optimum ink formulation. The shape of the dressings was printed as a circle with a diameter of 1 cm and cross-linked in 5%(w/v) CaCl2 solution. The release of insulin from wound dressing was evaluated by the Franz diffusion cell method.

Results: F4 ink formulation was selected (Figure 1a) as optimum according to the viscosity values, since the highest viscosity value was obtained with F4 as 7670 cP (Figure 1b). 3D printing process was carried out with this ink (Figure 1c). In vitro release studies showed that, approximately 80% release of insulin from wound dressing was observed in 8 hours and controlled insulin release was obtained during the 72 hours (Figure 1d).

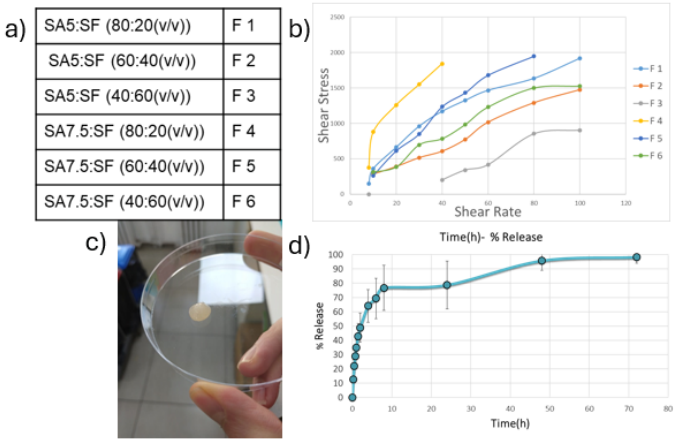

Figure 1. a: The content of ink formulations **b:** Shear stress-shear rate graphs of inks **c:** 3D printed insulin loaded wound dressing **d:** In vitro insulin release profile from wound dressing

Conclusions: Insulin-loaded sodium alginate-silk fibroin based wound dressings have been successfully produced using the 3D printing technology. Controlled release lasting 72 hours was achieved with the produced wound dressing.

Acknowledgements: This study was supported by Gazi University Scientific Research Projects Coordination Unit under grant number TGA-2023-8155. Tamer Tekin was supported by the Scientific and Technological Research Council of Turkey (TÜBİTAK) 2211-A National Doctoral Scholarship Program scholarship.

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OP088
PREFORMULATION OF NANOVACCINE LOADED DISSOLVING MICRONEEDLE FORMULATIONS

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Introduction: The skin, being the largest human organ and hosting a diverse array of immune cells near the circulatory and lymphatic systems, presents vast potential for intradermal vaccine delivery (1). Dissolving microneedle patches for intradermal vaccination provides virtually painless administration as the microneedles do not reach skin pain receptors (2). The aim of this study is to develop and characterize nanovaccine-loaded dissolving microneedle formulations.

Materials and Methods: Within the scope of the study, a polysiloxane mold was created to dissolving microneedle formulations and pre-formulation studies were carried out using polymers at various concentrations. Microneedles were produced by micro molding method. The formulation that produced optimum outcomes was chosen. OVA-FITC loaded NP was used to create this formulation utilizing a PDMS mold. NPs were produced by solvent evaporation method. SEM analysis and optical microscopy were used for analyzing the morphology of microneedles. For mechanical strength, texture analysis was used. Fluorescence method was used to determine the amount of encapsulation and in vitro antigen release.

Results: The results obtained showed that microneedles with smooth morphology were obtained according to optical microscopy results. As a result of the texture analysis, it was seen that the microneedles did not break despite the application of 325 N force. The produced microneedles seem to be sufficiently strong and able to puncture the skin. Scanning Electron Microscopy (SEM) imaging results are consistent with mechanical strength results. As a result of the in vitro release study, a prolonged release profile of up to 72 hours was obtained.

Conclusions: The results show that we have developed a microneedle formulation that can puncture the skin and deliver the loaded nanovaccine.

Acknowledgements: This study was funded by the Management of Scientific Research Projects of Ankara University (TSG-2023-2910).

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OP089
PREPARATION OF NANOFIBER FORMULATIONS OF 1,4-DIHYDROPYRIDINE-BASED CALCIUM CHANNEL BLOCKER

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Introduction: Hypertension is a chronic disease, characterized by persistent high blood pressure, that affects more than 1 billion patients worldwide (1). 1,4-Dihydropyridines (DHP) antihypertensive drugs are clinically used as L-type calcium channel blockers (2). DA8 is a DHP based calcium channel blocker. Nanofibers can be used as drug delivery systems to overcome solubility problems (3). In this study, DA8 loaded nanofiber formulations were prepared and physicochemical characterizations and cytotoxicity tests were carried out.

Materials and Methods: Electrospinning method was used to prepare nanofiber formulations. Fifteen mg DA8 was dissolved in PVP K90 polymer solutions with three different concentrations (10 %, 12 % and 14 % (w/v)). NF2 nanofiber formulation with 12 % PVP K90 polymer concentration was chosen to be used in physicochemical tests. For the physicochemical characterization tests, differential scanning calorimetry (DSC) was used to determine the thermal properties of the nanofiber formulation, PVP K90 polymer and DA8. The Fourier transform infrared (FTIR) spectra of the formulations and DA8 were recorded. L929 cell line was used in biocompatibility tests of the formulations and DA8.

Results: According to the DSC results, PVP K90 has peak between 50°C and 130 °C. While DA8 shows a sharp endothermic peak at 225°C-275°C, there is no obvious peak in the same range in DA8 loaded NF2 which means that DA8 may be in amorphous structure (4). FTIR results indicate that DA8 showed similar peaks with other DHP molecules. However, some characteristic peaks were decreased in NF2 formulation indicating that DA8 and nanofiber formulation may have interacted with each other. Biocompatibility study results were above 80% at all concentrations after 48h incubation.

Conclusions: DA8 loaded NF2 did not exert any toxic effect on the L929 cell line. According to the physicochemical analysis results, it was found that DA8 may have amorphous structure. There may be interaction between DA8 molecules and nanofiber formulation.

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OP090
DEVELOPMENT OF PROLIPOSOMAL DRUG DELIVERY SYSTEM IN CANCER THERAPY

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Introduction: Modulation of Nuclear factor erythroid 2-related factor 2 (NRF2) has emerged as an alternative approach to cancer treatment (1). Natural compounds that enable NRF2 modulation are preferred primarily, but their clinical use is limited due to poor bioavailability. Recent advances in pharmaceutical nanotechnology can overcome these disadvantages of natural NRF2 modulators and improve their in vivo efficacy. Liposomes are considered as ideal drug delivery systems, however, due to their low stability proliposomes have been developed as alternatives. Proliposomes are characterized by their dry, free-flowing characteristics, and liposomes are formed by contact with biological fluids in vivo or can be formed in vitro prior to administration using a suitable hydration fluid (2). In the current study, proliposomal formulations of plumbagin (PL), a natural NRF2 modulator, were developed and characterized.

Materials and Methods: A series of proliposome formulations (F1-F17) were prepared utilizing soy/egg phosphatidylcholine, maltodextrin, exhibiting distinct particle size distributions. To examine the influence of different preparation methodologies, both the slurry and film deposition-freeze drying methods were employed. The proliposomes were then assessed based on their production yield, consolidation properties, and morphological characteristics. After determining the production method for proliposome with the best characteristic, PL loaded proliposomes (PLP1-PLP6) were produced using different cholesterol and PL ratios.

Results: Proliposomal powder's Hausner index and Carr's index were less than 1.5 and 34,35 respectively which revealed good flowability. Empty liposomes derived from proliposomes were at nanoscale (293 -1331 nm) and negatively charged (-91,7 - -40,4 mV). This preliminary study revealed the advantage of using slurry method in further studies. PL-loaded proliposomes were successfully formed, achieving a maximum encapsulation efficiency of 52.8% (PLP2). The spherical structure of PLP2-derived liposomes was confirmed by TEM analysis. The in vitro dissolution tests revealed ~17% improved drug release via proliposomes compared to free PL at the end of a 24h release test.

Conclusions: This study shows successful encapsulation of PL in proliposomes which enhanced the solubility and dissolution rate of PL. The final formulation may enhance PL bioavailability, enabling its clinical use in cancer treatment.

Acknowledgements: This study was supported by TUBITAK in the scope of 2209-A University Student Research Projects Support Program (1919B012221260).

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OP091
EFFECT OF LAMOTRIGINE SOLID DISPERSIONS ON VIABILITY OF A549 AND RG-2 CELLS

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Introduction: Lamotrigine (LMT) is a second-generation anti-epileptic drug used to improve neuronal mechanisms (1). Also, recent studies on various cancer cell lines indicate that LMT-derived compounds show anti-cancer activity (2). Many approaches have been developed to overcome the oral bioavailability problems of drugs with poor aqueous solubility, such as LMT. Preparation of solid dispersions of the drug is one of these approaches (3). In this study, our aim was to investigate the effects of different carriers and ratios of carriers on the anti-cancer activity of LMT solid dispersions.

Materials and Methods: LMT solid dispersions were prepared by melting method. For this purpose, polyethylene glycol 4000 (PEG 4000), polyethylene glycol 6000 (PEG 6000), poloxamer 188 and poloxamer 407 were used in different ratios (drug to carrier ratios; 1:2 - 1:4 - 1:6 - 1:8 - 1:10). LMT solid dispersions were stored in a desiccator until cell culture studies were performed. The cell culture studies were carried out according to the procedure reported in the human lung cancer cell line (A549 cells) and rat brain glioblastoma cell line (RG-2 cells) (4). The samples (raw LMT, LMT solid dispersions, control-1(Dulbecco's modified eagle's medium supplemented with 10% fetal bovine serum, 50 U/mL penicillin and 50 µg/mL streptomycin), control-2 (Dulbecco's Modified Eagle Medium/Nutrient Mixture F-12 supplemented with 10% fetal bovine serum, 50 U/mL penicillin and 50 µg/mL streptomycin) were applied to the cells at 10, 20, 40 and 80 µg/mL concentrations for 24h. The results of cell culture studies were analyzed by two-way ANOVA test using the GraphPad Prism 8 statistical program.

Results: Cell viability was above 80% even at the maximum dimethyl sulfoxide (DMSO; 0.8%) used, indicating that DMSO did not cause a serious toxic effect on the cells. Cell viability for RG-2 cells was above 80% for nearly all samples and all concentrations except for the 40 µg/mL dose of solid dispersions prepared with PEG 6000 in a 1:6 ratio (78.2%).

Conclusions: Cell culture studies have shown that, in general, the prepared LMT solid dispersions do not have a significant toxic effect on cells.

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OP092
GASTRO RESISTANT LIPOPHILIC MATRIX TABLETS AS A SUPERIOR GENERIC ALTERNATIVE TO SOFT GEL CAPSULES

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Introduction: The pharmaceutical industry is dedicated to improving drug delivery systems to enhance patient compliance, product stability, and manufacturing efficiency. Soft gel capsules, have been widely used for their ability to encapsulate lipophilic drugs, ensuring rapid release and slow down the relase of hydrophilic drugs. Despite these advantages, soft gel capsules often face challenges, including higher production costs, complex manufacturing processes, and stability issues under certain conditions (1). To address these limitations, we have developed a generic lipophilic matrix tablet as an alternative to innovator sodium bicarbonate soft gel capsules. This novel tablet formulation aims to retain the therapeutic efficacy and bioavailability of the original soft gel capsule while offering enhanced stability, simplified manufacturing and potentially reduced production costs.

Materials and Methods: Tablets were developed and manufactured with a standard solid form manufacturing method the wet granulation technique, a process renowned for its simplicity and efficiency over traditional soft gelatin capsule production. The strategic incorporation of glycerol dibehenate as a matrix forming agent played a pivotal role in modulating the dissolution profile of a hydrophilic prototype drug, ensuring a controlled release profile that inspite of the high solubility characteristics of the active pharmaceutical ingredient. Additionally, the tablets were successfully coated with an enteric layer, conferring robust gastro-resistant properties. All specification are tested with validated analytical methods. Stability studies has conducted as per ICH requirements.

Results: The developed tablet formulations have been analyzed in a comparative manner against the reference product. The results have demonstrated that the tablets meet the specifications outlined in ICH Q6 for both release and the monitored stability period. Moreover, following acid resistance studies andı dissolution tests conducted under various conditions, the similarity coefficients (F2) with the reference product meet the requirements of the bioequivalence and bioavailability guidelines.

Conclusions: In conclusion, the lipophilic matrix tablet formulation developed through the conducted studies represents an alternative to the reference product in terms of efficacy and safety. Additionally, it offers advantages in production and patient compliance. Furthermore, this approach holds a pioneering quality, setting a precedent for future advancements in this field.

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OP093
SOLUBILITY AND DISSOLUTION ENHANCEMENT OF RACECADOTRIL BY INCLUSION COMPLEXATION WITH B AND HP-B CYCLODEXTRIN

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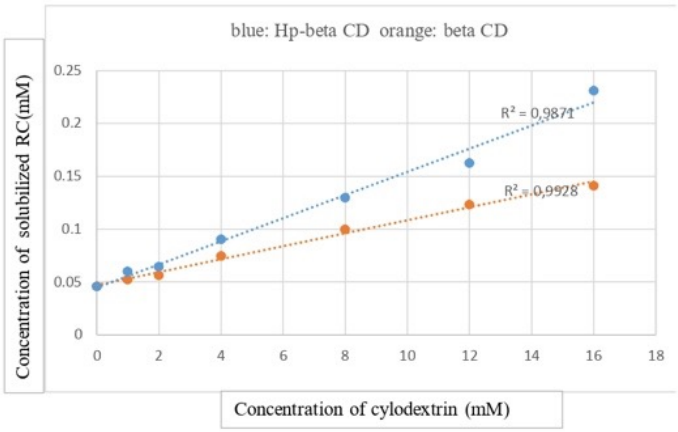
Introduction: Racecadotril(RC) is an orally administered enkephalinize inhibitor for the treatment of acute diarrhea and belongs to BCS class-II with low solubility and high permeability [1]. In this context, the present work focuses on the inclusion complexations (ICs) of RC with native cyclodextrins (CDs), beta (b) and 2-hydroxypropyl-beta (HP-b) and investigate effects on improved solubility and dissolution rate.

Materials and Methods: The phase solubility studies of RC (gift by ILKO Pharmaceuticals) with 1, 2, 4, 8 and 12 mM concentrations of βCD and HP-βCD (Wacker Chemie AG) were performed in line with the method reported by Higuchi and Connors to determine phase solubility diagram and apparent stability constant [2]. ICs of RC were prepared with β-CD and HP-β-CD at 1:1,1:2 different molar ratios by freeze-drying and kneading method. After that the obtained ICs were characterized by solubility, drug content, FT-IR analysis and in vitro drug release patterns.

Results: The phase solubility studies demonstrated that solubility of RC increased in the presence of both HP-β-CD and β-CD, thereby indicating AL type diagrams for both [3]. Stability constant (K) was found to be 130,31 M−1 for β-CD and 248,27 M−1 for HP-β-CD. Both K values were in range from 50 to 5000 M−1 therefore, ICs were considered suitable for solubility and stability improvements [4]. Water solubility results indicated that compared to HP-β-CD ICs, the solubility of RC was higher in β-CD ICs. Also β-CD ICs of RC using the lyophilization method increased RC solubility in water approximately four fold compared to pure drug. FT-IR spectrums showed the formation of ICs between RC and CDs. All ICs showed improved dissolution rates compared with pure drug. As a result, β-CD ICs obtained by lyophilization method had considerably higher effect on improvement solubility and dissolution rate of RC.



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OP094
DESIGN AND DEVELOPMENT OF A CUBOSOME DELIVERY SYSTEM CONTAINING PROTEINS

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Introduction: Cubosomes are biocompatible drug delivery vehicles made of liquid-crystalline nanoparticles with different amphiphilic lipid ratios. They accept many hydrophobic, hydrophilic, and amphiphilic drugs, improving entrapment and bioavailability (1). Since they may replace liposomes in drug delivery, cubosomes have become a prominent drug nanocarriers in oral, transdermal, ophthalmic, and chemotherapeutic drug administration (1). Cubosomes mainly consist of amphiphilic lipids such as Glyceryl Monooleate (GMO), Phytantriol, steric stabilizers and an aqueous solution, generally a buffer system or water (2). They are biocompatible, thermostable, biodegradable, and non-irritating (3). Their vast inner surface area allows for great drug entrapment capacity and simple, cost-effective manufacture compared to other lipid-based transporters (3). However, water-soluble drugs are less likely to remain in cubosomes due to their high fluid content and in vivo transmission and storage can leak active material from cubosomes (3). There are many examples of cubosomes filled with small compounds, but few with bigger chemicals and proteins (4). The aim of this study was to develop a model cubosome delivery system which can carry large compounds such as proteins; Griffithsin, an antiviral lectin in spesific.

Materials and Methods: Protein-loaded cubosomes were prepared with the top down approach without high temperature inputs by using GMO, ethanol, poloxamer 407, Tween 80 and a protein with a molecular weight of up to 14 kDa. The visual observations, light microscopy examinations, pH, particle size, zeta potential measurements, entrapment efficiency, release profiles and SEM examinations were conducted for characterization of cubosomes. Stability tests were performed at room temperature (22-25°C) and refrigerated conditions (4-10 °C).

Results: All characterization studies which were performed have proven that the cubosomes were successfully obtained. When refrigerated, cubosomes changed their appearances due to the cloud points of the non-ionics in the formulation. When left at the room temperature, their appearances have turned into their previous semi-transparent blueish colored liquid state. SEM images and the other values are summarized in Figure 1 and Table 1.

Conclusions: Cubosomes could be used to deliver larger molecules of proteins. Based on this information, this project can be further utilized as a delivery system of different molecular weight of proteins.

Acknowledgements: We are thankful to BASF and Active Bioworks for providing the materials used in this study.

Table 1: Summary of measurements

Time	Cubosome type	Mean Particle Size (nm)	PDI %	Mean Zeta Potential (mV)	pH	Appereance
T0	Empty cubosomes	134,72 nm	19,7%	-1,67 mV	7.10	Blueish white colored liquid
T0	Protein-loaded cubosomes	142,39 nm	20,8%	-1,3 mV	6.57	Blueish white colored liquid

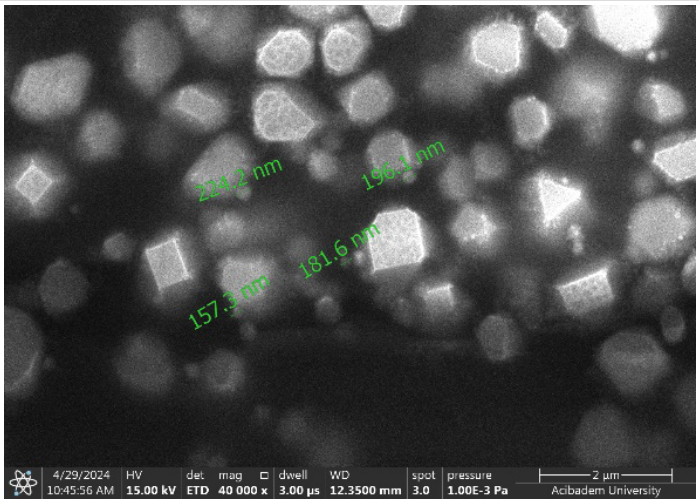

Figure 1: SEM images of cubosomes

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OP095
FORMULATION AND CHARACTERIZATION OF VITAMIN C CONTAINING SOLIDIFIED LIPOSOMES

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Introduction: Liposomes, lipid-bilayer vesicles, hold promise as effective drug delivery systems due to their versatility to accommodate various therapeutic agents and biocompatibility. Encapsulating Vitamin C (Vit C) in liposomes enhances its stability, protects its antioxidant properties, and facilitates controlled release, promising improved bioavailability and therapeutic efficacy (1). This study aims to improve the stability of vit C through solidified liposomal formulation. Key parameters such as zeta potential, particle size, polydispersity index (PDI), and morphological analysis has been performed.

Materials and Methods: Liposomes were prepared using the Reverse phase evaporation method with modifications. Phosphatidylcholine and cholesterol were dissolved in ethanol (lipid phase), while Tween 80 and Vitamin C were dissolved in double distilled water (aqueous phase). The lipid phase is added to the aqueous phase on magnetic stirrer at 1500 rpm for 1 hour. Maltodextrin was utilized to solidify the liposomes through the process of freeze-drying (2,3).

Results: The blank and Vit C loaded liposomes have been analysed, focusing on zeta potential, particle size, and polydispersity index (PDI). Both formulations exhibited favourable zeta potential values (-20.9 mV for blank, -18.0 mV for Vit C loaded liposomes), indicating electrostatic stability. Particle size analysis revealed uniform distribution, with mean sizes of 55.74 nm and 73.11 nm for blank and Vitamin C-loaded liposomes, respectively. After the addition of maltodextrin, sizes increased to 60 nm and 101.7 nm, while maintaining moderate PDI values. SEM images confirmed vesicular shape, and freeze-drying resulted in complete drying without any observable defects.

Conclusion: This study successfully formulated solid liposomes encapsulating VitC with favourable zeta potential, particle size distribution, and homogeneity. The achievement of complete drying during the freeze-drying process further validates the stability and robustness of the liposomal formulation. These findings show that Vit C can be successfully encapsulated into liposomal formulations. Future investigations can explore the efficacy and stability of these solid liposomes in greater detail, paving the way for their application in various pharmaceutical and biomedical fields.

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OP096
BRIDGING THE GAP FROM BIORELEVANT MEDIA TO SINGLE PHARMACEUTICAL SURFACTANT MEDIA: APPLICATION OF INTRINSIC AND FILM DISSOLUTION MODELS ON PIROXICAM

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Introduction: Piroxicam (PRX) is a poorly soluble drug. Biorelevant dissolution media such as fed state-simulated intestinal fluid version-2(FeSSIF-V2) are employed to anticipate in-vivo drug dissolution performance. However, the multiple component nature of biorelevant media is a barrier to their use in quality control (QC). QC media may best anticipate in-vivo product performance by mimicking in-vivo media, but preferably involve at most a single pharmaceutical surfactant, such as polyoxyethylene-10 lauryl ether(POE10) (1). The main objective was to predict PRX micelle diffusivity and surfactant-mediated dissolution into 2% POE10 and FeSSIF-V2 using film and intrinsic dissolution models, to bridge from biorelevant media to single surfactant media.

Materials and Methods: For each intrinsic and film dissolution, PRX dissolution into surfactant media was predicted. Predictions employed previously described models, which involved rotating disc and stationary disc dissolution testing(1,2). Dissolution rate was predicted for each rotating and stationary discs, in the absence(JD) and presence(JT) of surfactant. Relative to no surfactant dissolution, fold enhancement for intrinsic(Φintrinsic) and film(Φfilm) models were estimated.

Results: Piroxicam solubility increased 3.99(±0.07) and 3.85(±0.04)-fold in POE10 and FeSSIF-V2, respectively, compared to buffer. ff, fm, n and m were 0.245(±0.007), 0.755(±0.007), 6.93 and 420 for POE10; they were 0.254(±0.026), 0.746(±0.003), 16800 and 27000 for FeSSIF-V2. DD of free PRX was 112×10-7cm2/s. For intrinsic model, DD-M of drug-loaded POE micelle and FeSSIF-V2 mixed-micelle were 4.92x10-7(±0.072) and 0.56x10-7(±0.0055)cm2/s, respectively. JD into media without surfactant was 0.158(±0.002)µg/cm2/sec for intrinsic dissolution and 0.401(±0.005) µg/cm2/sec for film dissolution model. JT from DD-M and Deff were 0.211±0.0017 and 0.456±0.008µg/cm2/sec for POE10, 0.170±0.0019 and 0.407±0.004µg/cm2/sec for FeSSIF-V2. Φintrinsic and Φfilm were 1.38±0.004 and 1.14±0.002 for POE10, 1.09±0.0006 and 1.02±0.0001 for FeSSIF-V2. While 1.9% POE10 is needed to mimic drug solubility in FeSSIF-V2, only 0.2-0.3% POE10 is needed to simulate dissolution into FeSSIF-V2 reflecting the attenuating impact of slowly diffusing drug-loaded micelles.

Conclusions: Application of surfactant-mediated models indicates relative lower level of single surfactants can mimic biorelevant media. An outstanding question is whether we should mimic drug solubility or drug dissolution rate in biorelevant media.

Acknowledgements: This work was supported by TUBITAK-BIDEB2219(Project code:1059B192000617).

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OP097
PREPARATION OF BUPIVACAINE QUANTUM DOTS

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Introduction: Bupivacaine is a long acting local anesthetic(1). CDs are nanoparticles that are characterized by being in the form of nanoclusters and exhibit photoluminescence properties(2,3). This study aims to develop an easy one-step preparation method and show the possibility of increasing the effect using its quantum dot form. Bupivacaine carbon quantum dots(Bup-CDs) were successfully prepared and tested.

Materials and Methods: Bupivacaine was from Haver Pharma Drug Company, Istanbul, Turkey. Bup-CDs were prepared using the microwave synthesis method. Male Wistar albino rats obtained from SYLAB Experimental Animals Laboratory.

Bupivacaine solution and Bup-CDs were prepared with the same concentration. The study and the protocol were approved by the local ethical committee(044). Animals were anesthetized. The nerve was freed from the surrounding tissues from the sciatic notch to the branching area in the popliteal area by incisions. Test materials were injected at the specified dose under the fascia surrounding the sciatic nerve. Then, the superficial muscle planes were approximated and sutured with 4-0 silk thread. The skin was closed with metal clips.

Von Frey brush was used for mechanical stimulus pain testing(6). The heat-induced pain sensation test apparatus(Ugo Basile, Comerio, Italy) was preheated to 50°C before use. The time the animal placed on the hot plate to pull its foot and lick it within 60 seconds was recorded.

Results: Particle size and distributions, and zeta potential measurements of Bup-CDs are 8±0.213nm, 20%, and -40±0.142mV respectively. The optical and morphological properties of the prepared formulation are given in Figure 1.

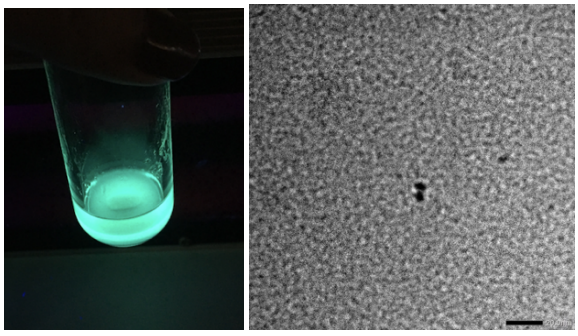

Figure 1. Image of Bup-CDs under UV and TEM.

Hot plate test and Von Frey Brush test *in vivo* study results of Bup-CDs applied to Wistar rats are given in **Figure 2.**

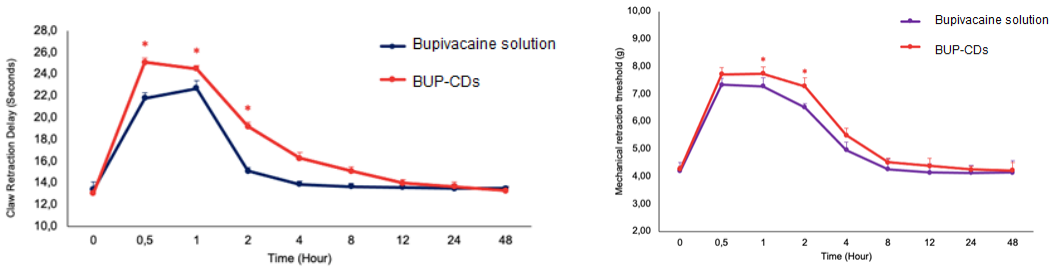

Figure 2. Von Frey Brush test results

Conclusions: It was shown that Bup-CDs were successfully prepared by a simple and one-step production. They are fluorescent and ready to use for both anesthetic effects and bioimaging. They are less than 10 nm in size. They were found to be more effective than that of the solution. These results show that they are biologically more effective and ready for other future purposes like bioimaging etc.

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OP098
AN EMULSION SYSTEM CONTAINING EXOSOMES WAS DEVELOPED USING A DROPLET-BASED MICROFLUIDIC SYSTEM

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Introduction: Exosomes are a type of membrane vesicles secreted into the extracellular space by most cell types. It has been determined that exosomes contain various biological entities such as proteins and microRNAs, and it has been shown that they are effective in performing many biological functions, especially in cell-cell communication. For this reason, studies are being carried out to use them as invaluable biomarkers for disease diagnosis, prognosis, and treatment (1). Exosomes obtained with challenging techniques also have storage problems after collection. Exosomes are usually stored at –80 °C, but studies have shown that exosomes are unstable in long-term storage under these conditions as well (2).

Microfluidic technology allows the encapsulation of biological active ingredients and the formation of emulsions with calibrated particles. Droplet microfluidics produce discrete droplets via immiscible multiphase flows within microchannels. In this way, any material desired to be encapsulated can be encapsulated away from all kinds of physical and chemical external factors that may cause the material to degrade (2).

Within the scope of this study, it was aimed to develop a system that will allow exosomes to be taken orally and stored at room temperature. For this purpose, mesenchymal stem cell exosomes were encapsulated by solid lipid using microfluidic technology as w/o emulsion and lyophilized after emulsion filling into enteric capsules.

Materials and Methods: Exosomes were obtained from Wharton Jelly using ultracentrifugation in PBS and used as an aqueous phase. A molten solid lipid with a melting point of 34–38 °C was used as the oil phase. MB5-Z500 microfluidic chips were used for W/O emulsion preparation. The obtained emulsions were collected in enteric capsules and lyophilized to dry the exosomes.

Results: Exosomes were placed into the emulsion system without degradation. It was observed that exosomes did not degrade after drying by lyophilization.

Conclusions: Promising results have been obtained in increasing the stability of exosomes, improving their storage conditions, and delivering them to the human body with drug delivery systems.

Acknowledgements: This study was supported by Anadolu University Scientific Research Foundation (Project ID: 1873) and a grant of TUBITAK (2210-A)

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OP099
PREPARATION AND CHARACTERIZATION OF TENOFOVIR DISOPROXIL FUMARATE AND EMTRICITABINE LOADED ZEIN BASED NANOFIBER FORMULATIONS FOR VAGINAL DRUG DELIVERY

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Introduction: Zein is an FDA-approved biopolymer isolated from corn that is biodegradable, biocompatible, easily available, non-toxic, non-allergic, and has low immunogenic effect (1). Daily oral administration of tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) combination is highly effective in preventing HIV transmission (2). The aim of this study was to develop and in vitro evaluation of vaginal TDF/FTC-loaded zein based electrospun nanofibers for topical pre-exposure prophylaxis.

Materials and Methods: Zein-based formulations were prepared at different concentrations in ethanol: distilled water (8:2). Polyvinylpyrrolidone (PVP) and polyethylene oxide (PEO) were used as mucoadhesive polymers to prepare electrospinning solutions with zein. The amount of TDF and FTC was kept constant in all formulations. The surface tension, viscosity and conductivity values of the polymer solutions were measured. Nanofiber formulations were produced by electrospinning method. The nanofiber formulations were evaluated for structural characterization using differential scanning calorimetry (DSC) and fourier transformed infrared spectroscopy (FT-IR). The contact angle measurements of formulations were carried out by optical tensiometer (Attension Theta Lite). Mechanical and mucoadhesive properties of nanofiber formulations were evaluated using Texture Analyzer. In vitro release studies of formulations were performed using Franz type diffusion cells.

Results: The viscosity, surface tension and conductivity values of the polymer solutions were found to be in a suitable range for electrospinning. Viscosity and conductivity values increased with increasing zein content. Characteristic peaks were seen in the FT-IR spectrum and DSC thermograms of the physical mixtures of the substances in the formulation while no peak was observed in the formulations. All formulations had hydrophilic properties. Low mechanical properties were observed due to the zein content in all formulations. TDF and FTC release from nanofiber formulations was observed at a ratio of approximately 65% TDF and % 50 FTC in 24 hours. An increase in mucoadhesion values due to PVP and PEO was observed compared to the formulation prepared with zein.

Conclusions: Due to the suitable mechanical and mucoadhesive properties, it was seen that zein-based formulations prepared with PVP were more promising in the vaginal application of TDF and FTC.

Acknowledgements: This study was supported by Gazi University Scientific Research Projects Coordination Unit under grant number 02/2020-17.

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OP100
DESIGN AND DEVELOPMENT OF WOUND HEALING DRESSING CONTAINING STORAX OIL PRODUCED BY ELECTROSPINNING

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Introduction: Wound healing is a process that occurs following the compromised integrity of tissue, wherein the anatomical and functional features of the injured tissues are reestablished (1). Storax oil is a balsam obtained from the trunk of the Liquidambar Orientalis Miller tree, which grows in Anatolia and is known by names such as Storax, Levant storax, Styrax liquidus, and Sweet gum. Storax balsam has been used by the local population since ancient times, primarily for medicinal treatments as an antiseptic, wound healer, antiparasitic agent (especially against scabies), and expectorant (1). It facilitates the rapid healing of skin diseases, wounds, burns, and cuts. Nanofibers are typically filaments with nano-scale diameters, commonly produced using electrospinning which involves the application of high electric power to draw a polymer solution from a needle capillary to a collector, creating a mesh of fibers (2) (Figure 2). Many different polymers are used for electrospinning as summarized in Figure 1.

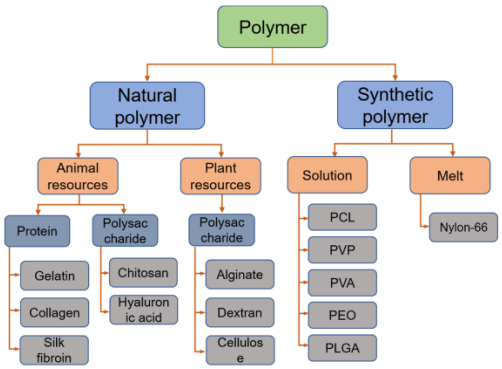

Figure 1. Polymers used for electrospinning.

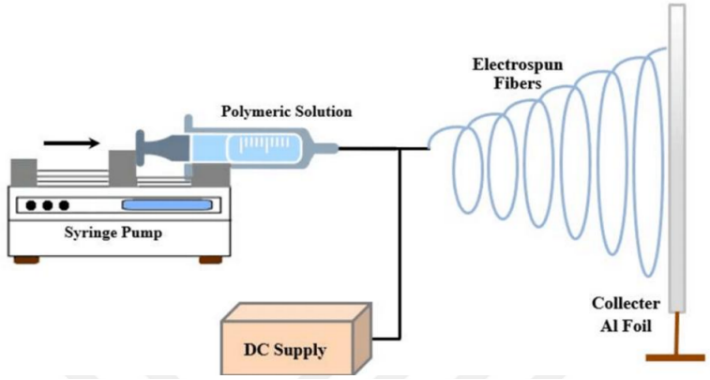

Figure 2. Electrospinning technique

Materials and Methods: PCL, Sodyum Alginate (Safic Care), Chitosan (low molecular weight, Aldrich) and Styrax (Köyceğiz Balı) are used as they were received. In order to see the effects of voltage applied to capillaries, solution flow rate, distance between syringe tip and collector, solution concentration, molecular weight of polimer,solution viscosity, surface tension, conductivity and temperature, electrospinning samples were prepared under different conditions and compositions. The characterisation tests included viscosity measurements, scanning electron microscopy (SEM) and transmission electron microscopy (TEM) analysis, wettability (contact angle), permeability, wound healing test, cell culture studies, encapsulation studies etc.

Results: Table 1 and Table 2 shows the solutions tried for electrospinning. Some of the solutions produced fibers meeting the required properties. The appearance and the surface properties of the candidate wound dressing are presented in Figure 3, Figure 4 and Figure 5.

Table 1.Electrospinning solutions in GAA

Sample No	Concentrations (wt%) in Glacial Acetic Acid (GAA90%)				
	PCL	CS	SA	PVA	Styrax
Study 1	6	3.1	-	-	1
Study 2	5	3	-	-	2
Study 3	5	3	-	-	2.9
Study 4	2	-	1	5.1	2.1
Study 5	1	-	1.2	5.2	2.2
Study 6	4	3	-	-	2
Study 7	3	-	1.1	5	2
Study 8	3	2	-	-	3.1
Study 10	0.5	1	-	-	2
Study 11	0.5	1	-	-	3
Study 12	0.5	-	1	4.5	2
Study 13	0.5	-	1	3.5	2

Table 2. Electrospinning solutions in Chlorophorm

Sample No	Concentrations (wt%) in Chlorophorm				
	PCL	CS	SA	PVA	Styrax
Study 14	20	10	-	-	3
Study 15	20	-	2	5	3.4
Study 16	15	4	-	-	3
Study 17	15.1	4	-	5.1	3.3
Study 18	15.1	-	1.1	4	3
Study 19	15	-	-	-	3.1
Study 20	10.1	1	-	-	3.1
Study 21	10.1	-	1	1	3
Study 22	15	-	-	-	5

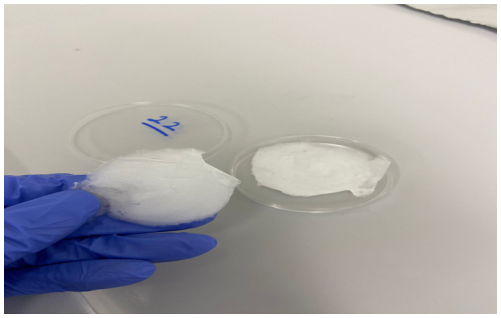

Figure 3

Figure 4

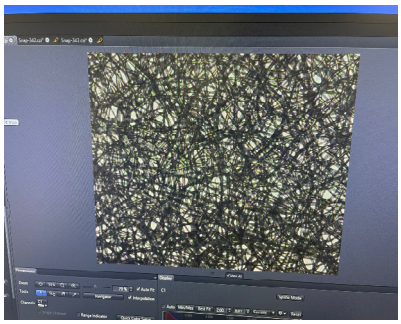

Figure 5

Conclusions: The wound dressing containing layers of fibers with storax and PCL in one layer, and gelling agents with PVA and Chitosan and PVA and sodium alginate in another layer provided good combinations. PLC -Storax layer provides a healing power while PVA / and gelling agents provide a good absorbance capacity to absorb the extracellular exudate and keeping the wound environment moist enough to help healing.

Acknowledgements: We are very greateful for Acıbadem Mehmet Ali Aydınlar University, Faculty of Engineering for letting us use their labratories for electrospinning experiments and for various tests we performed.

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OP101
BIOHESIVE DELIVERY SYSTEM FOR TOPICAL DELIVERY OF FUSIDIC ACID AGAINST MRSA SKIN INFECTIONS: IN VIVO EVALUATIONS

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Introduction: Methicillin resistant Staphylococcus aureus (MRSA) is a gram-positive bacteria which is the essential cause of community and hospital associated infections and commonly encountered in humans and animals, and usually colonizes the skin and mucosal membranes (1). Topical delivery of drugs against MRSA skin infections provides higher concentration of drug on the infection area and decreases the undesired effects (2, 3). In this study, we have evaluated in vivo the effect of the gel formulations we have developed for delivery of fusidic acid against MRSA infection in animal model.

Materials and Methods: Gel formulations were prepared using chitosan (with different molecular weight and degree of deacetylation), which is a bioadhesive biopolymer and which also exerts antimicrobial and wound healing effects. Subcutaneous infection was developed with clinical isolate MRSA4 in Balb/c mice (4). Beginning on Day 3 after the infection, formulations were applied topically on the infected area twice a day for 14 days, and at the end the treatment, animals were sacrified and tissue samples were collected. The level of inflammation was scored by histopathological examination. Bacterial load, myeloperoxidase (MPO) activity and cytokine levels (IL-1ß, IL-6, TNF-α, IL-17A) were also investigated.

Results: With the gel formulations containing fusidic acid, FA + gK3 ((7.1 x 104 CFU/mL) and FA + gM3 (3.7 x 104 CFU/mL)), significant decrease was observed on Day 14 in bacterial load when compared to that of control group (8 x 105 CFU/mL) ($p<0.05$), indicating increased wound healing. Ulceration and inflammation scores after treatment also supported wound healing effect of our formulations. Similarly, MPO activity in presence of chitosan (1.91 µmol/min) was observed to increase significantly when compared to that of the drug alone. With the formulations MPO activity was found to be higher than that of fusidic acid alone (4.09 µmol/min) ($p<0.05$), supporting the healing of the wound and infection. The expression of inflammatory cytokines (IL-1ß, IL-6, TNF-α, IL-17A) was significantly reduced following treatment with our formulations. In general, the type of chitosan was found to have no significant effect on wound healing.

Conclusions: We obtained promising results showing that the effect of fusidic acid was enhanced in presence of chitosan in experimentally induced wound. In conclusion, with our formulation based on chitosan, with bioadhesive and extended drug relase properties, it was possible to provide contact of the drug on the application site with longer period of time, allowing extended release of drug, consequently enhancing the effect of the drug.

Acknowledgements: This study was supported by Hacettepe University Scientific Research Coordination Unit (TUK-2022-19958)

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OP102
DEVELOPMENT OF LAVANDULA ANGUSTIFOLIA ESSENTIAL OIL CONTAINING MICROEMULGEL, IN VITRO CHARACTERIZATION AND ANTIMICROBIAL ASSAY

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Introduction: Lavandula angustifolia, one of the most promising medicinal plants, as a source of essential oils that are possesing a wide spectrum of biological activities (1). In this study we aimed to develop and evaluate the antimicrobial activity of microemulgels containing essetial oil of L. angustifolia collected from Adana, Turkey.

Materials and Methods: The *L. angustifolia* plant was collected from the Adana, Turkey. The essential oil was (LO) extracted via the steam distillation method, and analyzed by GC/MS device. For preparation of microemulsions, Labrafac WL 1349 was selected as an oil component, Tween 20 was used as surfactant, Transcutol was selected as the cosurfactant. Extractracted LO was added to microemulsions in 1% (w/w) (2). Globule size, PDI and zeta potential of the formulations were determined. Carbopol 940, 1% (w/w) was used for microemulgel development, microemulsion was incorporated into gel in the ratio of 1:1 (w/w). The antimicrobial effect of extracted LO, LO containing microemulsion and the LO containing microemulgel, was investigated by disc diffusion method by utilization of *S. aureus* ATCC 29213, *E. coli* ATCC 25922, *P. aeruginosa* ATCC 27853, *S. agalactiae* ATCC 12401, *E. feacalis* ATCC 29212 reference strains.

Results: Linalool, Linalyl acetate and trans-beta-Ocimene was found to be three highest amount of components in the extracted LO, by the GC-MS analysis. Globule size was determined as, 360.933±16.332, zeta potential as -0.033±0.002 and PDI as 0.320±0.001 for ideal ME formulation. It was found that LO and LO containing formulations showed significant antibacterial activity against the reference strains and pure LO exhibited the strongest antibacterial activity.

Conclusions: According to results of this study, L. angustifolia essential oil loaded microemulgels can be valued as a promising alternative for the treatment of topical infections.

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OP103
IN VIVO EVALUATION OF THE ANTITHROMBOTIC EFFECT OF CLOPIDOGREL NANOPARTICLES

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Introduction: Nanotechnology is the formulation of small particles with a size of 1-100 nm, leading to high surface-to-volume ratios, higher dissolution rate of the drug and enhanced bioavailability. Nanoparticles have more advantages in the treatment of chronic diseases through targeted and site-specific drug delivery (1).

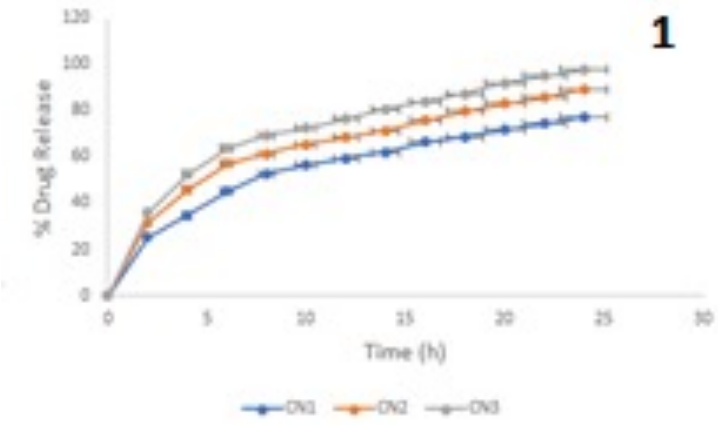
Clopidogrel is an anti-platelet drug that binds selectively to P2Y12 receptors on platelets thereby inhibiting adenosine diphosphate-induced platelets activation and aggregation. It is normally used to prevent the risk of heart attacks and strokes in predisposed hypertensive patients. Clopidogrel and other P2Y12 inhibitors are normally available as tablets with an oral bioavailability of about 50% (2). Hence the aim of this study was to formulate clopidrogel nanoparticles with improved bioavailability and better treatment outcomes.

Materials and Methods:

Materials: Clopidogrel pure sample (Cipla, India), Dichloromethane (Emsure, India), Eudragit RL 100 (Rhoma Pharma, Germany) and Sodium Alginate (Sigma, Germany).

Methods: Three (3) batches of clopidogrel nanoparticles were synthesized using the solvent evaporation method (2). Characterization of the synthesized silver nanoparticles was done using X-Ray diffraction spectrometer and scanning electron microscope. *In vitro* dissolution studies and *in vivo* antithrombotic studies were also done.

Results: The synthesized clopidogrel nanoparticles had a spherical shape with particle sizes of 69.14-134.29 nm, encapsulation efficiency of 38.32-47.41% and polydispersity index of 0.31-0.42. The nanoparticles had a zeta potential value of ≤+49.37 mV. The in vitro release studies showed that the clopidogrel nanoparticles released the drug in a sustained release manner simulating the Higuchi release model via Fickian diffusion mechanism (1). The formulated clopidrogel nanoparticles demonstrated significant antithrombotic effect in experimental rats (P<0.05).



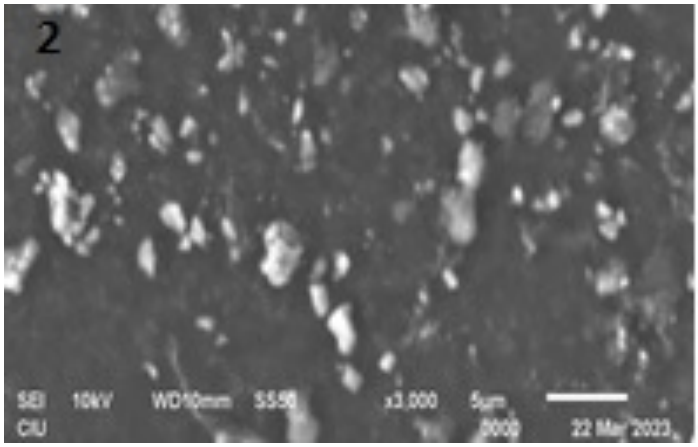


Figure 1: *In vitro* release profile and (2): SEM image of clopidrogel nanoparticles.

Conclusions: Clopidogrel nanoparticles were synthesized in this study which may offer better therapeutic outcomes compared to the conventional dosage forms (tablets) in the prophylaxis and treatment of acute myocardial infarction and ischaemic stroke.

Acknowledgements: The authors acknowledge the laboratory staff for their contributions to this research.

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OP104
SYNTHESIS AND BIOLOGICAL EVALUATION OF THIOSEMICARBAZIDE DERIVATIVES AS CARBONIC ANHYDRASE INHIBITORS

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Introduction: The imidazo[2,1-b]thiazole ring is present in a number of new thiosemicarbazide derivatives (1-3) that were developed and chemically produced at practical yields. The literature has reported on the broad range of pharmacological activity of imidazo[2,1-b]thiazole derivatives (1, 2). We present here the structure, synthesis, and carbonic anhydrase activity of novel imidazo[2,1-b]thiazole moiety bearing derivatives of thiosemicarbazide.

Materials and Methods: A mixture of 0.0075 mol 6-methylimidazo[2,1-b] thiazole-5-car-bohydrazide, 0.0075 mol appropriate isothiocyanates, and 10 ml of C2H5OH (96 %) was refluxed for 6-8 h. The crude product which precipitated on cooling was filtered and crystallized from ethanol. The synthesized compounds were investigated using 1H-NMR and ESI-MS.

Results: In this study, novel thiosemicarbazide derivatives were synthesized. The inhibitory effects of chemicals (1-3) and AAZ on hydratase activity of hCA-I and hCA-II enzymes were studied. The IC50 values for the compounds were computed at various concentrations while keeping a constant substrate concentration. The activity % values of enzymes were determined by measuring hydratase activity in the presence of various inhibitor doses (3).

Conclusions: In this study, novel thiosemicarbazide derivatives were synthesized. All produced compounds (1-3) were also tested for their capacity to inhibit human carbonic anhydrase isozymes. According to the findings, these derivatives could be considered promising lead drugs against hCA I/II enzymes.

Acknowledgements: The present work was supported by the Istanbul University Scientific Research Projects (Project No: TDK-2021-37637).

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OP105
DESIGN, SYNTHESIS AND ANTIVIRAL ACTIVITY OF 5-(TRIFLUOROMETHOXY)-1H-2-INDOLINONE DERIVATIVES

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Introduction: According to the World Health Organization (WHO, 2023), human herpes simplex viruses (HSV-1 and HSV-2), the most common viral disease agents, affect 67% and 13% of the population worldwide, respectively (1). Vaccinia virus (VV) is a complex enveloped virus and it has been the most widely studied virus along with being the source of modern smallpox vaccine (2). Methisazone (1-methy-1H-Indole-2,3-dione 3-thiosemicarbazone) is approved by Food and Drug Administration (FDA) in 1965 as the first antiviral compound for smallpox and vaccinia viruses for prophylactic use (3). Also, 1-ethyl-1H-indole-2,3-dione 3-(4-phenylthiosemicarbazones) had significant antiviral effects against HSV, VV, respiratory syncytial, yellow fever, and reovirus (4,5). In this study, the contribution of the isopropyl group at the position 1- of the indole ring to the antiviral effects was evaluated compared to the ethyl group.

Materials and Methods: 1-Ethyl/isopropyl-5-(trifluoromethoxy)-1H-indole-2,3-dione 3-(4-phenylthiosemicarbazones) (5a-d and 6a-d) were obtained by condensation of 5-(trifluoromethoxy)-1H-indole-2,3-diones with 4-phenylthiosemicarbazides. The structures of compounds were determined with spectral (IR, 1H-NMR and 13C-NMR) and analytical analyses. Compounds were screened against the strains of HSVs and VV in HEL cell cultures and cytotoxicities were determined. Molecular modeling studies were carried out with active compound 5d on HSV-1 (KOS) and HSV-2 (G). Free binding energies and theoretical IC50 values were calculated.

Results: 1-Ethyl substituted compounds 5a (R2: CH3), 5c (R2: F) and 5d (R2: Cl) had significant nontoxic effects against HSV-1 (KOS), HSV-2 (G), HSV-1 TK- KOS ACVr, and VV with EC50 values in the range of 2.3-5.6, 2.9-4.0, 1.5-2.3 and 4.0-8.9 µM, respectively. Only 1-isopropyl substituted compound 6c (R2:F) showed low antiviral activity against HSV-1 and HSV-2 with EC50 values at 50.0 and 15.0 µM, respectively.

Conclusions: The presence of ethyl substitution at position 1- of indole ring significantly changed its effectiveness against HSVs and VV compared to isopropyl group. While the methyl and halogens at the phenylthiosemicarbazone moiety increased the antiviral activity, the effect was significantly decreased with trifluoromethyl substitution.

Keywords: 1*H*-indole-2,3-dion, thiosemicarbazone, antiviral activity, molecular modeling.

Acknowledgements: This study was supported by TUBITAK 2211-A Scholarship Programme and by a grant of The Scientific Research Projects Coordination Unit of Istanbul University (TDK-2017-23300). We thank Prof. Lieve Naesens from Rega Institute for Medical Research (Leuven, Belgium) for the antiviral tests.

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OP106
SYNTHESIS OF SOME BENZIMIDAZOLE DERIVATIVES, EVALUATION OF CYTOTOXICITY AND MOLECULAR DOCKING STUDIES.

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Introduction: Cancer is one of the highest mortality and morbidity diseases in history. There is a need for researchers to synthesise new anticancer compounds due to the development of resistance to existing anticancer drugs. The aim of this study is to extend the findings of our previous study (1) and to synthesise new compounds in the light of these findings and to examine the cytotoxic activities of these compounds using the A549 and NIH3T3 cell lines.

Materials and Methods: Spectroscopic techniques were used to determine the structure of the synthesised compounds. The MTT assay based on the reduction of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium salt to the formazan product is used to determine the metabolic activity of living cells (2). Molecular docking studies were performed using an in-silico procedure as previously described (3, 4).

Results: According to the MTT assay, the IC50 values of compounds 4c and 4d were 26.469 µM and 20.137 µM, respectively. Compounds 4c and 4d have a selective toxic effect on cancer cells, although they were not as effective as the standard drug doxorubicin. The in silico study suggests that both compounds may have anti-cancer activity.

Conclusions: In this study, we designed and synthesized 2-(2-acetyl-1H-benzimidazol-1-yl)-1-arylethanone (3a-3d) and 1-methyl-3-phenyl-benzo[4,5] imidazo[1,2-a]pyrazine derivatives (4a-4d). The compounds we synthesised contain a benzimidazole ring structure, which is known to have anti-cancer activity, and were found to have no toxic activity.

Acknowledgements: Our authors express their gratitude to the AUBİBAM.

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OP107

SYNTHESIS AND CHARACTERIZATION OF NEW HEXAHYDROQUINOLINE DERIVATIVES, EVALUATION OF THEIR CYTOTOXICITY, INTRACELLULAR ROS PRODUCTION AND INHIBITORY EFFECTS ON INFLAMMATORY MEDIATORS

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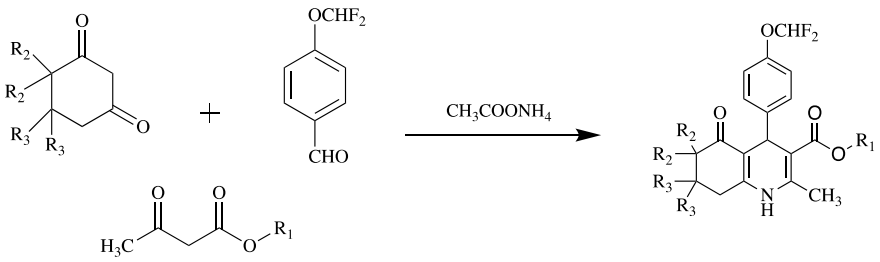
Introduction: Inflammation is known as the body's response to an injury or infection. Bacteria, viruses, stress, nutrients and environmental pollution are factors that trigger inflammation (1). Recent studies have shown that 1,4-DHP derivatives used as calcium channel blockers also have anti-inflammatory and immunosuppressive effects (2).

Materials and Methods: Compounds 1a-1e, 2a-2e and 3a-3e were synthesised by the Hantszch procedure under reflux (3).



Cell viability was determined as 100% in the control by MTT method. Based on the results obtained by MTT assays, Compounds 2d, 3b and 3e, which are the least cytotoxic compounds among the synthesized compounds in the 3T3 cell line and have good solubility under test conditions, were selected for biological activity assays.

Results: According to the biological activity results, compound 3b, which has the structure of ethyl 2,7,7-trimethyl-4-(4-difluoromethoxyphenyl)-5-oxo-1,4,5,6,7,7,8-hexahydroquinoline-3-carboxylate, had an inhibitory effect on most of the targets in the protein structure.

Conclusions: According to the results obtained, compounds with bearing bulky ester groups at 3rd and methyl groups at 7th of the hexahydroquinoline ring were found to be relatively active.

Acknowledgements: We acknowledge the research to Dr. Ilke Uğur Mario from Meddenovo Drug Design for molecular docking studies.

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OP108
NOVEL MANNICH APPLICATIONS ON UROLITHIN TYPE COMPOUNDS AND SCREENING BIOLOGICAL ACTIVITIES

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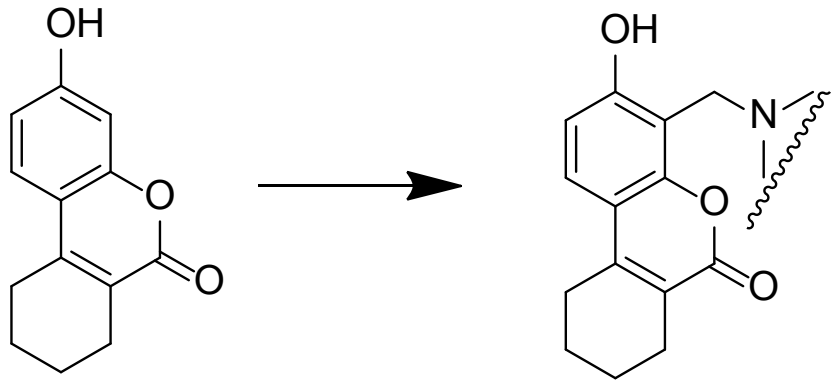
Introduction: Urolithins are hydroxy substituted benzo-[c]-chromen-6-one derivatives. They are the biotransformation products of ellagitannins and punicalagins. Many studies have shown so far diverse biological properties of these compounds (1). One aspect of our research relies on chemical modification of urolithins to obtain more active compounds. Within this content, we have come out a new methodology to design 4-aminomethyl substituted derivatives of urolithins. Different applications of Mannich reaction have been assessed and optimized (2). From this perspective, this presentation aims to describe the synthetic methodology achieved concomitant to biological activities obtained.

Materials and Methods: Diverse Mannich reaction applications have been followed including acidic and basic media. Anticholinesterase, and antioxidant activities have been conducted via Ellman's, and Orac Assay methodologies, respectively. Fluorescence quenching studies have also been performed to obtain iron binding characteristics.

Results: Microwave assisted methodology has provided the best synthesis option. The structures were identified employing 1HNMR, 13CNMR, IR and Mass analysis. Biological activities generated IC50s at low µM level in addition to comparable antioxidant properties to Trolox. Furthermore, iron chelating properties displayed the on-off probe characteristics of the systems created.

Conclusions: The application employed led to the generation of novel urolithin analogues with comparable/superior characteristics in comparison to standard molecules used.



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OP109

EXPLORING NOVEL HYDRAZONE/THIADIAZOL DERIVATIVES AS EGFR ENZYME INHIBITORS: SYNTHESIS, ANTICANCER POTENTIAL, MOLECULAR DOCKING AND DYNAMICS SIMULATION

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Introduction: Lung cancer is one of the leading causes of cancer-related mortality worldwide, with non-small cell lung cancer (NSCLC) accounting for most cases (1). Epidermal growth factor receptor (EGFR) inhibitors have emerged as promising therapeutic agents for treating NSCLC, targeting a critical pathway involved in tumor growth and progression (2). Nitrogen- and sulfur-containing heterocyclic compounds are of great importance in research and are widely used due to their established biological and pharmacological effects (3). This study focuses on the synthesis, characterization, and biological evaluation of a new series of hydrazone/thiadiazol derivatives with the potential to inhibit EGFR and exhibit anticancer activity.

Materials and Methods: A series of hydrazone/thiadiazol derivatives were synthesized following established synthetic protocols. Their chemical structures were determined through a combination of spectroscopic methods, including 1H NMR, 13C NMR, and high-resolution mass spectrometry (HRMS). The anticancer activity of the synthesized compounds was assessed using the MTT assay against the human lung cancer cell line.

Results: Molecular docking studies identified compounds 5f, 5g, 5j with high binding affinity for the active site of EGFR, suggesting their potential as effective inhibitors. In addition, molecular dynamics simulations demonstrated the stability of these compounds when bound to the EGFR active site. Experimental evaluation of anticancer activity showed notable to moderate inhibitory effects against the A549 cell line.

Conclusions: In summary, we synthesized a novel series of hydrazone/thiadiazol derivatives and confirmed their molecular structures using spectroscopic techniques. The compounds demonstrated varying levels of anticancer activity against the A549 lung cancer cell line. Computational studies provided insights into the binding affinity and stability of the compounds with respect to EGFR. These findings support the potential of these novel derivatives as candidates for further development in cancer therapy targeting EGFR.

Keywords: Thiadiazol, Hydrazone, EGFR, A549, Cancer

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OP110
A MOLECULAR DOCKING STUDY OF SOME ANTIOXIDANT COMPOUNDS WITH A POTENTIAL OF NOX-2 INHIBITION.

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Introduction: NADPH oxidases (NOX) are a family of membrane-bound enzymes that are mainly responsible for electron transport and production of reactive oxygen species (ROS). It is well-known that ROS are major players in oxidative stress-induced pathologies such as neurodegenerative diseases and cancer (1). NOX-2 is a member of this family that was first identified in neutrophils. It has been demonstrated to contribute to a number of dysfunctions including cardiovascular disorders as well as neuroinflammation, which puts NOX-2 inhibitors forward as a promising approach in treatment (1). It is hypothesized that some antioxidants may have an effect of inhibiting NOX-2. In this regard, we evaluated the potential interaction between NOX-2 and some synthesized compounds with antioxidant activity, through a docking study and compared them to GSK2795039, which is a selective NOX-2 inhibitor (2).

Materials and Methods: The ligand docking studies into NOX-2 protein (PDB ID: 8WEJ) (3) binding pocket were carried out by Autodock vina v.1.1.2 (4). Docking of the compounds were performed with MGL Tools v.1.5.7 (5). Discovery Studio Visualizer (BIOVIA, Dassault Systemes, v.21.1) was used to display the interactions of the ligands with the protein.

Results: Compounds were docked into the binding site of NOX-2 protein. Amino acids in the active site of NOX-2 and the interaction of the best docking poses of the compounds are obtained. HIS338 is the amino acid residue with which GSK2795039 interacts. Extra H-bond interaction was observed between amide N-H of the compound B and THR341. All compounds were compatible with the binding pocket, thanks to hydrophobic interactions between the aminoacid residues at the active site and the molecule. The fact that compound C is the most active compound in this series may be due to the interactions with the protein.

Conclusions: The co-crystallized ligand of the 8WEJ encoded protein was compared with the GSK2795039 and the common interaction was observed to be hydrogen bonding with HIS338. Considering that the selective NOX-2 inhibition of GSK2795039 occurs through HIS338, it is possible to hypothesize that the compound C may have an inhibitory effect on NOX-2.

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OP111

DESIGN, SYNTHESIS, MOLECULAR DOCKING AND MOLECULAR DYNAMIC STUDIES OF NOVEL BENZIMIDAZOLE-THIAZOLE DERIVATIVES AS POTENT SELECTIVE COX-2 INHIBITORS

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Introduction: In numerous studies, a positive correlation has been found between chronic inflammation and cancer (1). COX-2 enzyme activated by inflammation plays a crucial role in development of cancer associated inflammation, tumor progression, and metastasis (2). After considering the mentioned results and the numerous medical fields in which benzimidazole molecules are used, we designed and synthesized a series of benzimidazole derivatives containing thiazole ring as potential selective COX-2 inhibitors in this study.

Materials and Methods: For the synthesis of designed derivatives, o-phenylenediamine is cyclized to the benzimidazole ring by reaction with lactic acid. The oxidation of hydroxy ethyl moiety results in the formation of 2-acetyl-benzimidazole. The benzimidazole ring was derivatized from the first position using methyl, *p*-fluoro or *p*-bromo benzyl groups. Thiosemicarbazones were formed by the reaction of 2-acetyl benzimidazoles with thiosemicarbazide. The final products were obtained by the reaction of thiosemicarbazone derivatives with α-bromoacetophenones. The *in vitro* inhibitory potency of the compounds against COX-1/COX-2 was measured by using fluorometric screening kits. The molecular docking study was performed using the Schrodinger suite 2022-3 Glide XP (Extra Precision) module. Molecular dynamics (MD) simulations were performed using the GROMACS 2022.1 software package (3).

Results: A novel class of benzimidazole-thiazole products has been designed as potential inhibitors of COX, and the synthesized compound structures were verified using instrumental analysis techniques. Compound 8c (2-(2-(1-(1-(4-bromobenzyl)-1H-benzimidazole-2-yl)ethylidene)hydrazinyl)-4-(2-nitrophenyl)thiazole) has IC50 value close to celecoxib (IC50 0.132 µM) with 0.215 µM. The dynamic simulation results support the findings from the molecular docking studies and suggest that compounds 7b, 7c, 8b, and 8c may have the potential to act as potent and selective COX-2 inhibitors.

Conclusions: Among the derivatives containing *p*-substituted benzyl at the first position of benzimidazole, the derivatives containing a nitro group at the third and second positions were the most effective derivatives. Their IC50 values were lower than those of ibuprofen and nimesulide and close to that of celecoxib. When comparing the inhibitory properties against COX-1 and COX-2 enzymes, it was observed that the obtained compounds are more selective to the COX-2 enzyme.

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OP112
NOVEL HYDROXYPYRIDINONES AS ACETYLCHOLINESTERASE INHIBITORS FOR ALZHEIMER'S DISEASE

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Introduction: The incidence of neurodegenerative diseases is increasing with the rapid aging of the world population and the prolongation of life expectancy. Alzheimer's Disease (AD) is the main cause of dementia in the elderly and is a chronic and irreversible neurodegenerative disease that includes progressive deterioration of mental functions and behavioral disorders (1). Based on the hit compound KOJI MG84, whose anti neurodegenerative activity was reported in our previous studies and proven to cross the blood-brain-barrier an, using a multi-target ligand design approach, novel hydroxypyridinone (HPO) analogs were designed for the prevention and treatment of AD.

Materials and Methods: Mannich bases of HPO's were synthesized from kojic acid with four-step reactions (3, 4). The structures were identified by using appropriate spectroscopic methods. The acetylcholinesterase (AChE) inhibitory activities were screened by Ellman assay (5). Docking simulations were issued with Glide in standard precision mode. The highest ranking pose was selected for the generation of MD simulations (6).

Results: All the compounds were gained with quite yields and were found to inhibit AChE. Especially compound bearing 4-fluorophenyl piperazine moiety, had inhibition value of %96,84 and according to *in-silico* studies hydrophobic interactions were prominent with Tyr428 aminoacid of the enzyme.

Conclusions: Further studies with active compounds comparable to the standard drug Donepezil used in the treatment of AD will be carried out and their efficacy on AD models will be examined in vivo.

Acknowledgements: This study was supported by a grant of TUBITAK (122S035).

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OP113
NANOFLOWER SYNTHESIS FROM ALKANNA ORIENTALIS (L.) BOISS. VAR. ORIENTALIS (L.) BOISS. EXTRACT: COMPARISON OF POTENTIAL ANTIPARASITIC, ANTIOXIDANT AND ANTIMICROBIAL ACTIVITIES OF EXTRACT AND NANOFLOWERS

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Introduction: Alkanna species, popularly known as wound healers, are also known to be used in parasitic diseases (1,2). According a researches of metal nanoparticles using plant extract has increased recently due to its simple, scalable and non-toxic process. Particularly, nanoparticles and nanoflower (NFs) structures are frequently used in the field of biotechnology due to their unique shapes, properties and application areas (3,4). In the light of these innovations and based on the Leishmaniasis cases that cause serious infections in our country, it is also aimed to compare the antiparasitic, antioxidant and antimicrobial activities between the Alkanna orientalis extract and nanostructures by synthesizing copper and zinc nanoflowers structures from the obtained extract.

Materials and Methods: Aerial parts of A. orientalis were collected in appropriate seasons. After the aerial part extracts were obtained, their content analyzes were performed using High Pressure Liquid Chromatography (HPLC). Then, NFs was synthesized from these extracts. Scanning electron microscopy (SEM) for imaging and characterization of nanostructures; by X-ray diffraction (XRD) to illuminate nanostructures; and Fourier Transform Infrared Spectroscopy (FT-IR) will be used. Total phenolic and flavonoid contents of extract and NFs, DPPH (2,2-diphenyl-1-picrylhydrazyl) and ABTS (2,2'-Azinobis [3-ethylbenzothiazoline-6-sulfonic acid]-diammonium salt) radical scavenging effects, copper ion reducing activities (CUPRAC), catalytic activities and antileishmanial activities were studied in vitro. Antimicrobial activity studies were carried out using the broth microdilution method using ATCC strains of Staphylococcus aureus, Escherichia coli, and Candida albicans. For antiparasitic activity, culture medium using DMEM medium was prepared for Leishmania promastigotes. Ficoll gradient was applied to obtain metacyclic promastigotes. Infective promastigotes were stimulated with PMA to be phagocytosed by U937 cells. Following this, the factors were added to the medium at specified dose ranges to examine their cytotoxic effects on infected cells, and the results were evaluated with the MTT test.

Results: Methanol extract of *A. orientalis* examined in terms of total phenolic and flavonoid contents. In addition, secondary compounds were determined and detected using HPLC. Copper and zinc NFs were successfully synthesized and characterized by SEM, EDX, XRD and FT-IR analyses. All activities were determined for both the extract and NFs.

Conclusions: Herein, viability and cytotoxicity tests were performed to examine the effect of the obtained extracts on biological activity, and it was determined that these extracts had promising effectiveness in the treatment of this disease and inhibited the development of the parasite.

Acknowledgements: This study was supported by a grant of University of Erciyes (GAP-12253)

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OP114

ANTIMICROBIAL, ANTIBIOFILM, AND ANTIQUORUM SENSING ACTIVITIES OF CERIUM AND COPPER NANOPARTICLES GREEN SYNTHESIZED FROM HAZELNUT (CORYLUS L. SP) HUSK EXTRACT

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Introduction: The antimicrobial properties of cerium (CeNP) and copper (CuNP) nanoparticles synthesized using hazelnut husk extract were investigated against various microorganisms. Minimum Inhibitory Concentration (MIC) values were determined using the broth microdilution method against Staphylococcus aureus ATCC 25923 (MSSA), methicillin-resistant S. aureus ATCC 43300 (MRSA), Escherichia coli ATCC 25922, Klebsiella pneumoniae ATCC 13883, Pseudomonas aeruginosa ATCC 27853, and Candida albicans ATCC 10231. Additionally, antibiofilm and antiquorum sensing (anti-QS) activities were evaluated against P. aeruginosa PAO1 and Chromobacterium violaceum ATCC 12472, respectively.

Material and Methods: In 2023, plant material collected from Ordu in the Black Sea region was dried under suitable conditions and ground. 100 g of plant material was extracted using 1 L of methanol at 70°C for 45 minutes in an ultrasonic bath. The obtained methanolic extracts were filtered through pleated filter paper, then concentrated under low pressure and dried. A 0.1 M metal salt solution was prepared by mixing 200 ml of distilled water:methanol (4:1) solution with 10 g of dried plant extract, and the pH was adjusted to 12 using sodium hydroxide. The solution was incubated at 90°C for 4 hours. After cooling to room temperature, the solution was filtered through filter paper, and the remaining particles were dried at 90°C. The dried particles were transferred to a porcelain crucible and calcined at 500°C for 4 hours in a muffle furnace. The synthesized particles were characterized for morphology and particle size using an SEM device at Ankara University Nuclear Research Institute, for organic functional groups using an Agilent Cary 630 FTIR, and for optical properties using a Shimadzu 1601 UV-vis spectrophotometer.

Antimicrobial Activity: The nanoparticles were dissolved in sterile water and serial two-fold dilutions were prepared in Mueller Hinton Broth for bacteria and RPMI 1640 broth for fungi. Bacterial suspensions were adjusted to 5×10^5 CFU/mL and incubated at 35°C for 18-24 hours. For fungi, suspensions were adjusted to 0.5 to 2.5×10^3 CFU/mL and incubated at 35°C for 48 hours. Ciprofloxacin, gentamicin, and fluconazole were used as standard antibiotics.

Antibiofilm Activity: MIC values against P. aeruginosa PAO1 were determined, and sub-MIC concentrations were used in the crystal violet assay. Biofilms were formed in Brain Heart Infusion Broth with 2% sucrose and incubated at 37°C for 72 hours. After washing and air-drying, crystal violet was used to stain the biofilms, and optical density was measured at 620 nm.

Antiquorum Sensing Activity: MIC values against Chromobacterium violaceum ATCC 12472 were determined. The disc diffusion method was used to assess anti-QS activity, with bacterial cultures adjusted to 1.5×10^8 CFU/mL and incubated at 30°C for 24 hours. The presence of violacein inhibition zones was noted.

Results: CeNP (4 mg/ml): No antimicrobial activity was observed against any tested strains.

CuNP (4 mg/ml): Demonstrated MIC values of 250 µg/ml against MSSA, 125 µg/ml against MRSA, 1000 µg/ml against E. coli, and 500 µg/ml against C. albicans. No activity was observed against K. pneumoniae, P. aeruginosa, or C. violaceum.

Antibiofilm Activity: CeNP exhibited no biofilm inhibition activity against P. aeruginosa PAO1.

Antiquorum Sensing Activity: CeNP showed no anti-QS activity, as indicated by the absence of violacein inhibition zones in C. violaceum.

Conclusion: Copper nanoparticles synthesized from hazelnut husk extract exhibit selective antimicrobial properties, particularly against MRSA, MSSA, E. coli, and C. albicans. However, cerium nanoparticles did not show any significant antimicrobial, antibiofilm, or anti-QS activities. These findings suggest that CuNPs have potential as antimicrobial agents, while further modification may be necessary to enhance the efficacy of CeNPs.

Acknowledgements: Batuhan ÖZTÜRK thanks the financial support from the Technological Research Council of Turkey (TUBITAK) under the BIDEB/2247-C STAR

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OP115
INVESTIGATIONS OF THE ATOMISTIC INTERACTIONS BETWEEN P53 WITH HIV-1 TAT PROTEIN

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Introduction: HIV encodes several accessory proteins, each of which plays a distinct and specific role. Among them, HIV-1 Tat (transactivator of transcription) is perhaps the most prominent one (1). During infection, this protein interacts with various proteins, one of which is p53. The interaction between Tat and p53 is perplexing because their roles appear to be contradictory. While p53 functions to induce apoptosis, Tat's goal is to ensure the survival of HIV (2). To comprehend the interaction mechanisms of these proteins, we investigated their atomic-level interactions using in silico methods.

Materials and Methods: Tat (PDB code: 1K5K, model 1) and p53 (PDB code: 2J0Z) were docked using four different protein docking web servers. Consensus binding modes were identified from the first 10 models generated by each server, resulting in the determination of four distinct models for the Tat-p53 complexes. Subsequently, these models underwent molecular dynamics (MD) simulations in three replicas each.

Results: Out of the 12 models, in simulation 1, model_ZDOCK, the binding energy was notably lower at -46.6 kcal/mol, rendering it the most favorable among all the considered models. In this particular model, the initial contact between the two proteins involves numerous interactions between Tat(47–57) and p53(326-342). Subsequently, these interactions are further refined by additional interactions, where Tat binds to p53 through residues 1-31. This observation is consistent with findings in the existing literature (3).

Conclusions: Given that the interaction between p53 and Tat plays a pivotal role in determining whether infected cells survive or undergo apoptosis, the development of compounds targeting this protein complex holds significant therapeutic promise. We believe that our model, which aligns with key findings from the literature, could be instrumental in designing such therapeutics.

Acknowledgements: The authors kindly acknowledge TUBITAK/TRUBA for computational time.

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OP116
COMPARISON OF MOBILITY-BASED SEPARATION TECHNIQUES AND MASS SPECTROMETRY FOR BIOTHERAPEUTICS IDENTITY CONFIRMATION.

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Introduction: Pharmaceutical biotechnology requires rigorous analysis, employing different methods for thorough characterization. Electrophoretic techniques are valuable for analyzing high molecular mass molecules, particularly complex glycoproteins, assessing their heterogeneity and size (1). Meanwhile, mass spectrometry provides precise molecular mass determination of intact molecules regardless of molecule size or shape (2). The study aimed to evaluate quality of biotherapeutics and address molecular mass determination challenges using orthogonal methodologies.

Materials and Methods: Six different commercially available biologics consisting of gonadotropins of human and recombinant origin were studied using gel electrophoresis and microchip capillary electrophoresis and MALDI-TOF-MS. Enzymatic glycan release was performed to investigate the glycan bulk influence on the complexity and exact molecular mass determination of gonadotropins under study.

Results: High complexity and extreme macro- and microheterogeneity, typical for glycoproteins were demonstrated. In gel electrophoresis biotherapeutics showed a typical behaviour, with many bands and complex spot patterns migrating at different Mr and pI, while in microchip capillary electrophoresis broad peaks at high mass range were obtained due to the glycan effect. These effects were consistent across various glycoproteins with different glycan compositions. After the release of oligosaccharide, narrower peaks were obtained and at lower mass ranges, corresponding to the real molecular mass. However, MALDI-TOF/MS enabled the exact molecular mass determination of the intact biomolecules.

Conclusions: Gonadotropins exhibited significant heterogeneity, with electrophoretic migration behavior typical of biologics. This orthogonal approach proved to be capable for the accurate molecular mass determination and of purity and structural integrity of such complex biologics as gonadotropins.

Acknowledgements: This study was supported by CEEPUS and HERAS.

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OP117
SYNTHESIS OF NOVEL 5/2-SUBSTITUTED-1H-BENZIMIDAZOLE DERIVATIVES AND DOCKING STUDY AGAINST CYCLOOXYGENASE ENZYME

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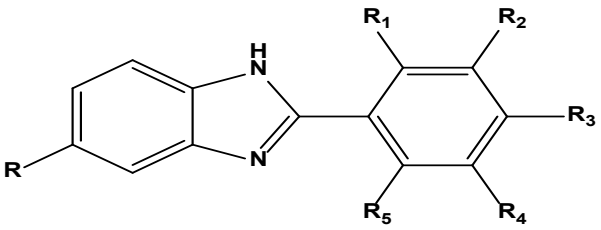
Introduction: The benzimidazole moiety meets the minimum structural requirements for anti-inflammatory drugs (1). Because of their ability to inhibit COXs, enzymes involved in the manufacture of essential inflammatory mediators known as prostaglandins, benzimidazole-based compounds are extremely useful as anti-inflammatory and analgesic medicines (2). This study is aimed to design, docking, and synthesizing new 5/2-substituted-1H-benzimidazole derivative H1-H13.

Materials and Methods: The new benzimidazole derivatives (H1-H13) were synthesized and elucidated using Mass Spectroscopy, 1H NMR, and 13C NMR Spectroscopy. Benzyl alcohol or 4-chloro-phenol was reacted with 2-nitro-5-chloroaniline to prepare 5-(benzyloxy) or 5-(4-chlorophenoxy)-2-nitrobenzamine, respectively, then reduced using SnCl/HCl in ethanol to obtain 4-benzyloxy or 4-(4-chlorophenoxy)-ortho-phenylenediamine derivatives. The sodium metabisulfite salts of the respectively substituted aromatic benzaldehydes were heated in DMF with 4-benzyloxy or 4-(4-chlorophenyloxy)-ortho-phenylenediamine at 135 0C for 6 hours, the solid (compounds H1-H13) was obtained after addition of cold water and purified by column chromatography. The docking study was conducted for all compounds against cyclooxygenase enzyme (COX-2) (PDBID 5IKQ) to test the anti-inflammatory activity of the synthesized compounds using Cresset Flare software. The co-crystallized ligands were used to define the grid box and indomethacin was used as a positive control.

Results: All the synthesized compounds except H1&H4 having a binding energy score ranging from -11.14 to -8.06 kcal/mol which are better than control compound indomethacin (-7.98 kcal/mol).

Conclusions: The compounds H1-H13 could be good drug candidates with COX-2 inhibition properties and can be used as lead compounds for discovery a new anti-inflammatory drug.



1-13

H1;R_3=OCH_3, **H2**;R_1=OCH_3, **H3**;R_1=R_4=F, **H4**;R_3=CN, **H5**;R_3=COOH, **H6**;R_1=R_5=Cl, **H7**;R_1=OCH_3, **H8**;R_3=OCH_3, **H9**;R_2=R_3=OCH_3, **H10**;R_1=R_3=OCH_3, **H11**;R_1=R_5=Cl, **H12**;R_1=R_3=Cl, **H13**;R_1=R_4=F. **H1-H6**;R=benzyloxy, **H7-H13**;R=4-chlorophenoxy.

Figure: Structure of compounds **H1-H13**.

Acknowledgements: This study was supported by a grant of BAP, ANKARA UNIVERSITY.

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OP118
SYNTHESIS, STEREOCHEMICAL ANALYSIS AND ANTIMICROBIAL ACTIVITY OF COX INHIBITOR-AZOLE HYBRIDES

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Introduction: Nonsteroidal anti-inflammatory drugs (NSAIDs) alleviate inflammation and pain through the inhibition of cyclooxygenase (COX) enzymes (1). Besides these therapeutic utilizations, NSAIDs have been reported to display moderate antimicrobial activity (2). In this study, we designed novel potential antimicrobial agents by linking some NSAIDs (ibuprofen, flurbiprofen, and naproxen) to various azole rings (pyrazole, imidazole, triazole, and benzimidazole) via hydrazone functionality.

Materials and Methods: The hydrazone linker was introduced into the chemical scaffold of the title molecules by the reaction between hydrazides obtained from NSAIDs and in-house synthesized azole-carrying benzaldehydes. The structures of the target compounds were elucidated by spectral methods. The NOESY spectra and stereochemical analyses performed using DFT method. Finally, some derivatives were demonstrated to inhibit Candida albicans filamentation and/or bacterial communication system known as quorum sensing.

Results: Stereochemical analyses confirmed the presence of the target molecules as a mixture of E(C=N)-E(N-N)-synperiplanar and E(C=N)-E(N-N)-antiperiplanar conformers in DMSO-d6 solution. Some derivatives in this series of COX inhibitor-azole hybrids presented inhibition capacity on Candida albicans filamentation and/or on quorum sensing. For COX inhibitor-azole hybrids with antimicrobial potency, naproxen appeared to be the most appropriate NSAID, while bulky benzimidazole was not found as a preferable azole ring.

Conclusions: With its biological and conformational data, our study offers a valid approach for the stereochemical analysis of N-acylhydrazones derivatives with various pharmacological activities.

Acknowledgements: This study was supported by the BAGEP Award of the Science Academy the Ministry of Science, Technological Development and Innovation of the Republic of Serbia, 451-03-47/2023-01/200042.

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OP119
METABOLOMICS STUDIES ON RANUNCULUS DAMASCENUS BOISS. & GAILL. SPECIES AND DETERMINATION OF ANTIMICROBIAL ACTIVITY

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Introduction: The World Health Organization (WHO) has identified antimicrobial resistance as one of the top ten worldwide public health challenges that humanity faces (1). Thus, the demand for prospective antibacterial medications emerges. The objective of this study was to determine the antibacterial activity of *Ranunculus damascenus* Boiss & Gaill., in addition to their metabolite profiles and effects on different bacteria strains.

Materials and Methods: The methanolic extract of aerial parts from plant material is used for this study. Minimum Inhibitory Concentration (MIC) testing was used to determine the antimicrobial properties of plant extracts at concentrations ranging from 1024-2 µg/ml against reference strains of *Staphylococcus aureus* ATCC 25923, *Streptococcus epidermidis* ATCC 35984, *Escherichia coli* ATCC 25922, and *Klebsiella pneumoniae* ATCC 13883. The standard was followed in the Clinical and Laboratory Standards Institute (CLSI) M07 determination (2). LC-QTOF-MS is used to determine the metabolic profile.

Results: The MIC values of *S. aureus* ATCC 25923 and *K. pneumoniae* ATCC 13883 were determined to be 128 µg/ml, *S. epidermidis* ATCC 35984 was 64 µg/ml, and *E. coli* ATCC 25922 was 32 µg/ml. Totally, 44.254 metabolites were detected, and 260 of them were identified. Flavonoids are the most numerous group of identified compounds.

Conclusions: *R. damascenus* species showed the highest antimicrobial effect on *E. coli* ATCC 25922. Also, the contribution of metabolites to the activity was discussed.

Acknowledgements: This study was supported by a grant of Afyonkarahisar Health Sciences University Scientific Research Projects Coordination Unit (Project No: 22.KARIYER.005)

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OP120
CYCLOTRICHIUM ORIGANIFOLIUM (LABILL.) MANDEN & SCHENG.: PHYTOCHEMISTRY AND BIOLOGICAL CHARACTERISTICS

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Introduction: C. origanifolium, also known as "dağ nanesi", is commonly used in Eastern and Southern Anatolia as a flavoring agent in soups and salads, as well as a popular herbal tea. (1,2) It was aimed to assess antimicrobial, antioxidant, antidiabetic, and anticholinesterase effects of methanolic and aqueous extracts, as well as essential oils obtained from flowering aerial parts of C. origanifolium.

Materials and Methods: Aqueous and methanol extracts were obtained from flowering aerial parts of C. origanifolium. Essential oils were analyzed by GC-MS/MS. Antioxidant (DPPH scavenging activity, ABTS scavenging activity), total quantification (phenolic and tannin), antidiabetic (α-Glucosidase and α-Amylase), anticholinesterase (Acetylcholinesterase and Butyrylcholinesterase) and antimicrobial (disc diffusion) activities were analyzed. Biosafety of extracts was also investigated using Ames/Salmonella and Allium test methods.

Results: Isomenthone was main component of flowering aerial part essential oil with 52.4%. Extracts showed no significant inhibition on α-glucosidase but showed moderate inhibition on α-amylase. Essential oil showed mild inhibition on acetylcholinesterase (11.84%) and butyrylcholinesterase (16.93%). Methanol extract exhibited the best antioxidant potency according to both ABTS and DPPH assays. Total phenol and total tannic acid contents were higher in methanol extracts. Essential oil showed strong antimicrobial effect on Pseudomonas aeruginosa, Enterococcus faecalis at a concentration of 10 µl.

Conclusions: This study can be considered an important step towards understanding pharmacological and biological properties of C. origanifolium. However, further studies are necessary to fully understand the medicinal and industrial potential of the plant.

Acknowledgements: Enes TEKMAN thanks graduate program and scholarship supported by TUBITAK.

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OP121
PHARMACOGNOSTIC STUDIES ON GLECHOMA HEDERACEA L.

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Introduction: Ethnobotanical studies have shown that Glechoma hederacea L. which is also known as "ground ivy" is traditionally used for wound healing as well as some other biological activities, but there have not been enough studies on its wound healing effect (1). In our study, in vitro antioxidant, anti-inflammatory and wound healing activities and cytotoxicity of the aerial parts of G. hederacea were investigated**.**

Materials and Methods: The antioxidant capacities of the extracts prepared with ethanol, methanol and distilled water from the aerial parts of G. hederacea were evaluated by DPPH and ABTS radical scavenging activity assays and total antioxidant capacities of the extracts were determined; while wound healing activity and anti-inflammatory effect were tested using scratch assay and nitrite inhibition assay, respectively. For the evaluation of cytotoxicity, MTT assay was conducted. Besides, total phenol and total flavonoid contents were determined by spectrophotometric methods.

Results: As the result of DPPH radical scavenging activity method, the highest antioxidant capacity were found for ethanolic (IC50=0.2110±0.0107 mg/mL) and methanolic (IC50=0.1636±0.0174 mg/mL) extracts. The highest antioxidant capacity was determined by ABTS radical scavenging activity method the highest value for total antioxidant capacity in ethanolic extract with IC50 values of 0.2295±0.0085 mg/mL and 134.3145±8.4834 mg AAE/g dry extract, respectively. The methanolic extract of G. hederacea showed remarkable anti-inflammatory activity at the highest dose (1 mg/mL). Moreover, nitrite inhibition of G. hederacea extract at their highest concentration was approximately 60%. Methanol extract did not exhibit any cytotoxic effect on L929 and RAW264.7 cell lines up to a dose of 1 mg/mL. It was found that G. hederacea has the potential for wound healing activity, but the methanolic extract (83%) did not possess significant wound healing activity compared to the control (80%). Total phenol content was found to be highest in methanolic extract (85.1740±4.6693 mg GAE/g dry extract), while total flavonoid content was highest in ethanolic extract (42.5651±1.9937 mg QE/g dry extract). HPLC analyses revealed that the alcoholic extracts contained rutin, chlorogenic acid and rosmarinic acid.

Conclusions: It was suggested that G. hederacea extracts, which were found to exhibit significant antioxidant capacity and anti-inflammatory activity and contain phenolic compounds, have a potential in terms of wound healing activity.

Acknowledgements: Part of this study was supported by TÜSEB (34091).

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Tablo 1. Effects of different concentrations of the extract on the viability of RAW264.7 macrophage cells and the effects of the different concentrations of the extract on nitrite levels and % nitrite inhibition in RAW 264.7 cells stimulated with 1 µg/mL LPS. (*p<0.001)

Groups	Dose	Cell Viability (%)	Nitrite Level (µM)	Nitrite Inhibition (%)
Ctrl		109.34 ± 0.33	3.20 ± 1.39	-
Ctrl+LPS		100.04 ± 0.12	56.61 ± 5.09	-
L-Name	100 µM	92.45 ± 2.11	31.66 ± 0.81*	43.87 ± 3.54
Indomethacin	100 µM	93.13 ± 1.69	29.07 ± 2.03*	48.57 ± 2.00
G. hederacea extract (mg/mL)	0.125	99.33 ± 1.07	37.37 ± 1.51*	33.78 ± 3.46
	0.25	93.66 ± 1.41	34.03 ± 2.14*	39.79 ± 1.66
	0.5	91.04 ± 2.68	30.99 ± 0.34*	45.00 ± 4.26
	1	80.09 ± 1.97	22.65 ± 1.90*	59.69 ± 5.75

Tablo 2. Antioxidant capacity of the *G. hederacea* extracts and controls.

***G. hederacea* extract**	**DPPH IC_{50} (mg/mL)**	**ABTS IC_{50} (mg/mL)**	**Total antioxidant capacity (mg AAE/g dry extract)**
MeOH	0.1636±0.0174	0.2399±0.0226	125.2198±8.8168
EtOH	0.2110±0.0107	0.2295±0.0085	134.3145±8.4834
Water	0.2628±0.0340	0.2710±0.0265	74.8707±6.9952
Control			
Ascorbic acid	0.0129±0.0005	0.0321±0.0009	-
BHT	0.2393±0.0072	-	-
Trolox	-	0.0384±0.0025	-

Tablo 3. Phytochemical constituents of the *G. hederacea* extracts.

***G. hederacea* extract**	**Total Phenol Content (mg GAE/g dry extract)**	**Total Flavonoid Content (mg QE/g dry extract)**	**Rosmarinic Acid (%)**	**Chlorogenic Acid (%)**	**Rutin (%)**
MeOH	85.1740±4.6693	32.8976±1.2673	0.5988±0.0041	0.1739±0.0004	0.0633±0.0001
EtOH	80.8687±2.2789	42.5651±1.9937	0.2116±0.0008	0.0917±0.0002	0.0384±0.0001
Water	71.1298±2.4003	15.5038±0.3518	-	-	-

OP122
INULA AUCHERIANA DC. AERIAL PARTS EXTRACTS: GC-MS ANALYSIS, ANTIOXIDANT ACTIVITIES AND ETHOSOME FORMULATIONS

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Introduction: The genus Inula, is a member of Asteraceae family, encompasses 77 recognized species globally(1). Previous studies have identified major constituents of Inula sp. as eudesmanolides, guaianolides, germacranolides, xanthanolides, dimeric sesquiterpenes, flavonoids and phenolic acids. Inula confertiflora is traditionally utilized for treatment of viral skin infections, wounds, and eczematous lesions, while Inula helenium is known for its therapeutic properties in management of neoplasms, wounds, freckles, and dandruff(2). Ethosomes are soft and flexible lipid vesicles which consist of phospholipid, alcohol, and water. They have demonstrated significant potential in treatment of skin diseases because of their enhanced skin penetration and ability to improve the permeation of active pharmaceutical ingredients(3). In the study, we aimed to elucidate phytochemical content, antioxidant activities of ethanol extract and various fractions obtained from aerial parts of Inula aucheriana DC. and to develop Inula aucheriana loaded ethosome formulations which might be applied in management of skin diseases and cosmeceutical applications.

Materials and Methods: Aerial parts of Inula aucheriana were extracted with ethanol using percolator. Extract was subsequently fractionated with petroleum ether, dichloromethane, and ethyl acetate in order of increasing polarity. Petroleum ether fraction was subjected to GC-MS analysis. All fractions and ethanol extract were evaluated for their antioxidant activity using DPPH and FRAP assays(3,4).

Inula aucheriana loaded ethosome formulations were prepared using *(i)*thin film hydration method and *(ii)*ethanol injection methods, followed by sonication for 10 min. Formulations consisted of 2 %(w/w) *Inula aucheriana,* 30%(w/w) ethanol and phosphatidylcholine ranging from 1 to 3%(w/w). Then, they were characterized in terms of particle size, polydispersity index (PDI) and zeta potential.

Results: Results of GC-MS analysis identified several terpenic compounds, which have potential to enhance skin penetration of active pharmaceutical ingredients. Additionally, ethyl acetate fraction exhibited the highest antioxidant activity, which is particularly significant to protect of skin cells from damage and aging. Ethosomes prepared using thin film hydration method exhibited smaller size (175.2±1.8 nm) and lower PDI (0.404±0.016) compared to those prepared by ethanol injection method (224.1±13.2 nm, 0.496±0.092). Increase in phosphatidylcholine concentration resulted in decrease ethosome sizes and PDIs in both methods. The zeta potentials exhibited similar values, approximately 3-4 mV.

Conclusions: Inula aucheriana loaded ethosome formulations might be presented a promising delivery system for management of skin diseases and cosmeceutical applications. This might be attributed to their potential for enhanced skin penetration, facilitated by terpenic compounds in Inula aucheriana and ethanol in ethosomes, as well as antioxidant activity exhibited by Inula aucheriana.

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OP123
IN VITRO EVALUATION OF THE CYTOTOXIC EFFECTS OF POLYSTYRENE MICRO AND NANOPLASTIC PARTICLES IN L929 CELL LINE

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Introduction: Microplastics (MPs) are tiny fragments of plastic originating from several sources, such as clothing microfibers and plastic waste. The diameter of a microparticle (MP) is less than 1 µm and the plastics with a size range of 1-100 nm are called nanoplastics (NPs). Through intake and respiration, micro and nanoplastics (MNPs) can enter the body and build up in bodily tissues. The atmosphere, freshwater, land ecosystems, and the ocean have all been found to contain MNPs. Ingesting food may allow micro and nanoplastics into the human digestive system and when they go up the food chain into organisms, they may damage cells. Because MNPs can be mixed with food, oral exposure has become a crucial method for understanding their effects. Research suggests that MNPs may be harmful to the human gastrointestinal system. The purpose of this study was to investigate, at different doses, the cytotoxic properties of MNPs containing polystyrene that were isolated from disposable coffee cup lids in L929 cell line.

Materials and Methods: To evaluate the cytotoxicity of MNPs, MTT assay was conducted in L929 cell line and exposure times were determined as 24h, 48h and 72h. The used concentrations of MNPs ranged between 5-1000 µg/mL and the IC50 values were calculated.

Results: In almost all microplastic treatment conditions, the trend followed a dose-dependent decrease in cell viability, and overall decreases were observed at the highest dose at all treatment times. The results showed that a cytotoxic effect of microplastics was observed in L929 cells after exposure.

Conclusions: In this study, the cytotoxic effects of polystyrene MNPs particles on the L929 cell line were evaluated through in vitro experiments. This suggests that particle size plays an important role in the extent of the observed cytotoxic effects. Furthermore, extending this assessment to other cell lines and in vivo models will provide a broader understanding of the health effects of polystyrene micro- and nanoplastics.

OP124
CORRELATION BETWEEN MIR-29A-3P EXPRESSION LEVEL AND DOSE NORMALIZED DESMETHYLDIAZEPAM LEVEL IN INDIVIDUALS DIAGNOSED WITH ALCOHOL WITHDRAWAL SYNDROME

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Introduction: Alcohol Withdrawal Syndrome (AWS) is characterized by some clinical symptoms such as anxiety, tremor, insomnia and tachycardia (1). In cases, where AWS is not fully treated, treatment of alcohol use problem may become difficult due to uncontrollable cravings and relapses. Diazepam is the drug of choice for the treatment of AWS. Diazepam forms its active metabolite N-desmethyldiazepam (nordazepam) under CYP2C19 enzyme catalysis (2). One of the reasons for the differences in metabolite levels of diazepam between individuals is the variations in gene expression encoding enzymes and proteins involved in diazepam pharmacokinetics or pharmacodynamics. MicroRNA (miRNA) is an epigenetic mechanism that alters gene expression by degradation of target mRNA or suppression of translation (3).

Materials and Methods: This study aimed to determine whether there is a correlation between miR-29a-3p expression levels and desmethyldiazepam levels in individuals diagnosed with AWS. For this purpose, 55 men who were in the alcohol withdrawal period and started detoxification intervention with oral diazepam at doses varying according to the severity of withdrawal were included in the study. MicroRNA miR-29a-3p expression level was measured by quantitative real-time PCR (qRT-PCR) method, and plasma desmethyldiazepam levels were measured by High Pressure Liquid Chromatography (HPLC). miR-29a-3p expression level was calculated as 10.21 (IQR: 4.6-21.63), and the dose normalized desmethyldiazepam value was calculated as 0.068 mg/day ng/mL (IQR: 0.03-0.12).

Results: There was a statistically significant and negative correlation between miR-29a-3p expression level and dose normalized nordazepam (r2=-0.359, p=0.07).

Conclusions: Our study showed that miR-29a-3p may have an effect on CYP2C19 gene expression. Additionally, this study provides the first data on the relationship between diazepam treatment and miRNA levels in the Turkish population.

Key Words: Alcohol Withdrawal Syndrome, miR-29a-3p, CYP2C19, Desmethyldiazepam, Pharmacogenetics

Acknowledgements: This study was supported by Ankara University Scientific Research Projects Coordination Unit with grant no TDK-2022-2763.

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OP125
PUBLIC AWARENESS OF ASBESTOS HAZARDS AND DEMOLITION PRACTICES IN EARTHQUAKE-AFFECTED AREAS

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Introduction: Asbestos fibers exhibit their harmful effects by adhering to the lung (1). Long-term exposure to asbestos fibers causes asbestosis, pleural plaques, mesothelioma, and lung cancer.(2) Following a recent earthquake disaster in Turkey in 6 February 2023, hundreds of buildings were demolished in many provinces. The demolition of heavily damaged and moderately damaged buildings is still ongoing. During this process, asbestos dust released during the demolition of buildings in which asbestos was used in construction is very harmful. These processes, which are carried out without adequate precautions, will inevitably accelerate the development of cancer in the coming years. To measure the level of awareness of our people on this issue, whether they take precautions during the demolition process or not, and most importantly, to learn their situation and their level of being affected by this process, we conducted this survey. The purpose of this cross-sectional survey is to make our people realize that we are in a situation after such exposure and to take the necessary precautions.

Materials and Methods: Data for this cross-sectional survey was collected through an electronic survey between the respondents. The questionnaire consisted of questions aimed at measuring demographic information, level of awareness against asbestos exposure, measuring their level of exposure to asbestos dust released during the demolition process, smoking status of the participants, and questioning their smoking status.

Results: 704 participants, 70.9% female and 29.1% male, participated in the study. Most of the participants lived in the earthquake zone.59.9% of the participants had never heard the concept of asbestos before, while 40.1% stated that they had heard about it. On the other hand, 89.5% of the participants stated that they do not know whether asbestos is used in their buildings or not ($p<0.05$).

Conclusions: The results of this study indicate that there is a significant lack of awareness about the dangers of asbestos among the public. This is particularly concerning in areas affected by the earthquake, where asbestos-containing buildings are more likely to be demolished. Public awareness campaigns and education programs are urgently needed to raise awareness about the dangers of asbestos and to promote safe demolition practices. This is essential to protect public health and prevent future asbestos-related diseases.

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OP126
STUDIES ON NOVEL PHTHALIMIDO-BENZENESULFONAMIDE HYBRID AS PROMISING A-GLUCOSIDASE INHIBITOR

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Introduction: As per WHO report, diabetes is a fast-growing major health problem and T2DM constitutes about 80%-90% of all diabetic cases (1). One of the therapeutic approaches in the treatment of T2DM is the inhibition of carbohydrate digestive enzymes such as α-glucosidase which is considered as a prime target to discover and develop new antidiabetic agents (2). Various heterocyclic molecules have been employed for exploring new antidiabetic agents as they are promising tools that have been studied extensively by medicinal chemists for the design and development of new entities (3). In the search for new antidiabetic compounds with heterocyclic scaffold, we aimed to design synthesize and evaluate α-glucosidase inhibitory activity of 4-phthalimido-N-(5-chloro-2-pyrdinylamino)benzenesulfonamide derivative (Figure 1).

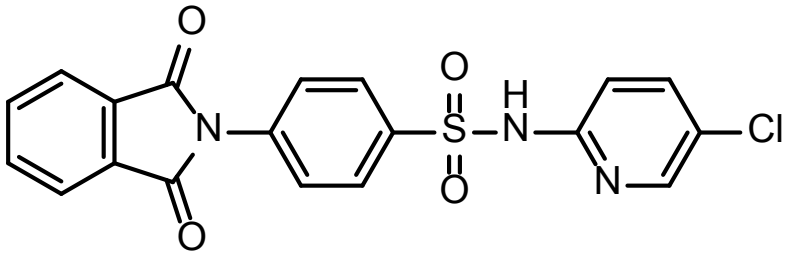

Figure 1. Structure of the target compound

Materials and Methods: The target compound was synthesized via three-step synthesis procedure according to the literature (4). IR, 1H NMR and MS spectral analysis were used to confirm the structure of the target compound. Biological activity studies were performed spectrophotometrically in order to determine in vitro α-glucosidase inhibition in comparison to acarbose as reference drug (5). In addition, molecular modeling studies provided key interactions with the active site of the enzyme.

Results: In this preliminary study, 4-phthalimido-N-(5-chloro-2-pyrdinylamino)-benzenesulfonamide derivative has been synthesized to explore its inhibitory activity towards α-glucosidase. According to the screening results the final compound exhibited significant IC50 value which was comparable to the reference drug acarbose. Furthermore, molecular docking studies revealed informative clues for the ligand-enzyme binding interactions.

Conclusions: As a result, it can be suggested that this derivative may serve lead compound for further studies in the search for novel α-glucosidase inhibitors.

Acknowledgements: The authors thank to Dr. Güneş ÇOBAN for molecular modelling studies and to the Pharmaceutical Sciences Research Centre (FABAL) at Ege University, Faculty of Pharmacy for spectral analysis and biological studies of the compound.

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OP127
INVESTIGATION OF NEW BENZIMIDAZOLE DERIVATIVES AS TOPOISOMERASE 2 INHIBITORS

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Introduction: Cancer ranks as one of the primary contributors to global mortality. Throughout 2022, close to 20 million individuals were diagnosed with cancer, resulting in approximately 9.7 million deaths worldwide (1). Various anticancer therapies have focused on targeting human topoisomerase enzymes in their design and development processes (2). DNA topoisomerases are classified into two classes Topo I and Topo II, depending on the number of broken strands of DNA by the enzymes in one reaction cycle. All type of topoisomerases indicates their biochemical functions by catalyzing DNA cleavage and relegation. Topoisomerase II (Topo II) is subdivided into two isoforms: Topo IIα and Topo IIβ. While Topo IIα shows high expression in actively proliferating cells, Topo IIβ is considered nonessential for proliferation. The benzimidazole core has gained prominence in cancer research due to its expansive anticancer capabilities and versatile mechanisms for inhibiting tumors, along with its straightforward synthesis procedures allowing for the creation of diverse derivatives(3). In this study, we aimed to demonstrate the activity of benzimidazoles on topoisomerase 2 enzyme.

Materials and Methods: Thiosemicarbazide derivatives were obtained by reacting benzimidazole hydrazides and corresponding isothiocyanates with reflux in an ethanol medium. Cyclization reaction of these compounds with sulfuric acid, sodium hydroxide or mercuric (II) acetate resulted in the formation of thiadiazole, triazole and oxadiazole derivatives, respectively. Molecular docking studies were performed to explain the potent Topo II inhibition of the compounds studies to explain high affinity.

Results: Compared to doxorubicin, oxadiazole derivatives were found to be more active and the most active compound among oxadiazoles with a docking score of 10d(N-(4-fluorophenyl)-5-[(2-phenyl-1H-1,3-benzimidazol-1-yl) methyl]-1,3,4-oxadiazol-2-amine).

Conclusions: These results suggest that novel benzimidazole derivatives targeting topoisomerase 2 enzyme are a promising strategy for cancer therapy.

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OP128
QUINOXALINE DERIVATIVES AS ALPHA-GLUCOSIDASE INHIBITORS: SYNTHESIS AND BIOLOGICAL EVALUATION

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Introduction: Diabetes mellitus is a major health problem and cause various complications (1). Due to the life-threatening complications, it is necessary to effectively control postprandial hyperglycemia and treat diabetes. α-Glucosidase inhibitors are widely used to control postprandial blood sugar levels and manage diabetes effectively. Moreover, these inhibitors exhibit potential in targeting other diseases such as HIV and cancer (2,3). However, currently used inhibitors have undesirable side-effects, making it necessary to discover new inhibitors (4). For this purpose, we synthesized a new quinoxaline-hydrazone derivative and evaluated its biological activity in vitro.

Materials and Methods: Chemistry: The quinoxaline-hydrazone derivative, compound KH14, was synthesized in three steps. Firstly, o-phenylenediamine and oxalic acid were heated to obtain quinoxaline-2,3-dione. Then, this intermediate was refluxed in hydrazine hydrate to obtain 3-hydrazinylquinoxalin-2-one. Finally, 3-hydrazinylquinoxalin-2-one and 4-hydroxybenzaldehyde were refluxed to yield KH14.

Biological Activity: Different concentrations of the KH14 and enzyme were added to wells, incubated at 37°C. After incubation, the substrate was added, and spectrophotometric measurements were taken at 405 nm. Standard; DMSO, reference; acarbose. IC_{50} values calculated using the GraphPadPrism.

Results: The structure of KH14 was confirmed using IR and 1H NMR spectroscopic methods. The α -glucosidase inhibitory activity of KH14 was determined spectrophotometrically in vitro, with its IC50 value was calculated as 0.413±0.048 mM, while this value was determined as 1.211±0.08 mM for acarbose.

Conclusions: The results of in vitro studies show that the synthesized quinoxaline-hydrazone derivative (KH14) exhibits significant α -glucosidase inhibitory activity. Upon evaluating the IC50 values, it is evident that KH14 inhibits α -glucosidase more effectively than the reference acarbose, making it a promising choice for future research. Our effort will continue to do so.

Acknowledgements: This study has supported by a grant of Ege University, Office of Scientific Research Projects (ID-31974)

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OP129
NOVEL 2-MORPHOLINOMETHYL-BENZIMIDAZOLE-1-SULFONAMIDE/ CARBOXAMIDE AS CARBONIC ANHYDRASE İNHIBITORS: SYNTHESIS, STRUCTURE CHARACTERIZATION AND MOLECULAR DOCKING STUDIES AGAINST İSOFORMS I, II, IX AND XII

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Introduction: Carbonic anhydrases (CAs) are a diverse group of zinc metalloenzymes found ubiquitously in the body. In humans and other primates, there are fifteen CA isoenzymes, each with distinct subcellular locations, catalytic activities, and sensitivities to different inhibitors. CA inhibition has been clinically utilized for decades to treat a wide range of conditions, including glaucoma, edema, epilepsy, obesity, neuropathic pain, and various neurological disorders. Recent research has shed light on the role of certain CA isoforms, particularly CA IX and XII, in tumor progression and metastasis, particularly in hypoxic cancers (2). Among the known inhibitors of CAs, sulfonamides and their analogs (such as carboxamides and sulfamides) stand out as potent agents. The ubiquity of CAs, the selectivity of the inhibitors for certain isoforms is a crucial issue to be reached in a drug development campaign to target a disease without relevant side effects (3). Within the scope of this study, synthesis, structure characterization, and molecular modeling studies of new 2-morpholinomethyl-benzimidazole-1-sulfonamide/carboxamide compounds against carbonic anhydrase I, II, IX, and XII isoforms were carried out.

Materials and Methods: Two new compounds derived from benzimidazole were synthesized according to literature, their structures were proven, and docking was done for CA inh.

Results: The interactions of two new drug molecule candidate compounds, whose structures have been proven, in the target enzyme/receptor region were determined using molecular modeling methods.

Conclusions: It was observed that the two compounds had a better binding mode and interacted with a larger number of amino acid residues in the enzyme active sites.

Acknowledgments: This study was supported by a grant of TUBITAK (2209a-1919B012305552)

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OP130
MUCOADHESIVE IN-SITU GELLING FORMULATION OF TRIPLE DRUG COMBINATION FOR BUCCAL APPLICATION: DEVELOPMENT AND IN-VITRO EVALUATION

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Introduction: In the present study, a triple therapeutic formula consisting of hydrocortisone sodium succinate (HSS), lidocaine HCl (LID), and dexpanthenol (DEX), is developed. Poloxamer polymers (P188 and P407) were used to create the thermosensitive in-situ gelling system, with carbopol incorporated for enhanced mucoadhesiveness. This formulation aimed to leverage the synergistic effects of the three components to provide comprehensive therapeutic benefits for oral lichen planus, targeting inflammation, pain relief, and tissue repair.

Materials and Methods: The study investigated drug, polymer, and preservative compatibility using differential scanning calorimetry, evaluated rheological and mucoadhesive properties of the triple drug formulation, characterized its liquid-to-gel transition, monitored drug release using a Franz diffusion cell apparatus over 6 hours, and assessed the physical and chemical stability under different storage conditions to determine shelf-life.

Results: The developed triple drug formulation exhibited promising characteristics, the developed formulation was liquid at room temperature and turned into gel at 35.1 ± 0.90 °C, consistence with low viscosity at 25 °C of 252.5 ± 0.0016 cPAS, and higher viscosity of 338.0 ± 0.007 cPAS at 37 °C, ensuring ease of administration and allowing retention of the drug formulation upon application and prolonged therapeutic activity. The formula exhibited an onset release of 31.7%, 36.0%, and 40.0% for HSS, LID, and DEX, respectively at 15 min and more than 80% released at 6 hours. The physical and chemical stability of the developed formula was investigated at three storage conditions of 5±3 °C, 25±2°C /60% ±5% RH, and 40±2°C/75%±5% RH. The formula demonstrated acceptable stability for 1 month when stored at 5±3 °C.

Conclusions: The study highlights the potential of an in-situ gelling drug delivery system for the treatment of oral lichen planus. However, further optimization and stability testing at room temperature (25±2°C /60% ±5% RH) will be the focus of future research to enhance the practical application and shelf life.

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OP131
INVESTIGATION OF LIPID NANOPARTICLE :PDNA COMPLEX INTERACTIONS WITH BIOLOGICAL MATERIAL

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Introduction: Low transfection efficiency and high toxicity are two of the major challenges in non-viral gene delivery. Serum nucleases and biological polyanions lower the efficiency of pDNA therapeutics. In this study, novel lipid nanoparticle (LNP):pDNA complexes were developed as non-viral gene delivery systems with the aim to investigate their protective effect against protease degradation and polyanionic stress.

Materials and Methods: LNP's were prepared by freez drying- rehydration-sonication method using DOPC, DOTAP and Cholesterol at different molar ratios (Oner et al., 2021). Samples were frozen at -80°C, dried under deep vacuum for 24 h, rehydrated in HEPES buffer and probe-sonicated. LNP:pDNA complexes were formed at RT by incubating LNPs with pDNA at N/P ratios between 0.5 and 12. Complex integrity and pDNA stability in the presence of serum were assessed for different incubation periods (Zhang et al., 2017). Complexes were incubated with heparin to test the resistance to anionic stress. FBS and heparin treatments were analyzed by agarose gel electrophoresis (Yadav et al., 2021).

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Cytotoxicity studies were performed on PC-3 cells. Cells were treated with complexes and cell viability was assessed using resazurin.

Results: Obtained LNPs effectively complexed pDNA above N/P ratio of 3. No pDNA decomplexation was observed in the presence of 10% and 50% FBS. Intentional release of pDNA revealed supercoiled pDNA conformation for all complexes. Complexes at higher N/P ratios were more stable against polyanionic stress. The complexes were non-toxic on PC-3 cell line at the tested concentrations.

Conclusions: The prepared LNP's successfully formed complexes with pDNA and protected it against serum protease degradation. pDNA was not released from the omplexes at N/P 12 ratio. All complexes were biocompatible and suitable for transfection.

Acknowledgment: This study was supported by Ege University Scientific Research Projects Department, project no. 30842.

OP133
SIMULTANEOUS DETERMINATION OF AMOXICILLIN AND POTASSIUM CLAVULANATE WITH NEW HPLC METHOD AND PHOTODEGRADATION VIA MAGNETIC ZNO NANOPARTICLES

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Introduction: The semi-synthetic antibiotic amoxicillin (Amox) and the β-lactamase inhibitor potassium clavulanate (Clav) are widely used in combination in the treatment of bacterial infections (1). Many different formulations containing these two antibiotics are available in our country. Antibiotic resistance, which develops due to the increasing human population and frequent use of antibiotics, is an important issue in the field of health worldwide (2).

In the present work, single HPLC method for analyses of amoxicillin and potassium clavulanate mixtures was developed and validated according to ICH guidelines. The pharmaceutical contaminants degradation can be carried out by photodegradation using ZnO-Fe_3O_4 magnetic nanocomposite photocatalysts.

Materials and Methods: Amoxicillin trihydrate, potassium clavulanate standards were given kindly by DEVA Holding A.Ş. (Tekirdag, Turkey). All analytical reagents were purchased from Merck and Sigma. Agilent 1200 HPLC system coupled with DAD detector were employed for simultaneous determination of Amox and Clav. Ace Hİ chroma C18 column (5 µ 4.6 × 250 mm) was used. Mobile phase is mix of ethanol and pH:3 buffer solution (10:90 v/v) at a flow rate of 1.0 ml/min with detection at 230 nm. ZnO-Fe_3O_4 magnetic nanocomposite was synthesized with some modifications in the method of Saridevi et al. (3). The synthesized catalytst was caharacterized with Fe-Sem, Sem , XRD and FT-IR techniques.

Results: A new, simple, specific, sensitive, rapid, accurate and precise RP-HPLC method was developed for the simultaneous of Amox and Clav. The calibration curves was linear in the concentration of 1.0-20 µg/ml for Amox and 2.0-50 µg/ml for Clav. The intra and inter day variation was found to be less than 5%. The mean recovery of the drugs from the pharmaceutical samples and waste water were found above 98%. The photodegradation of amox and Clav was monitored exploiting HPLC device. The photocatalytic degradation efficiency of ZnO-Fe3O4 the hybrid material for antibiotics was between 80% and 100%.

Conclusions: The proposed HPLC method was found to be simple, rapid, sensitive, precise and accurate for the simultaneous determination Amox and in pharmaceutical formulationsand waste water. The using of magnetic ZnO nanoparticles are promoting practical application for wastewater treatment.

Acknowledgements: This study was supported by Erciyes University Scientific Research Projects Coordination Unit with TYL-2024-13760 research project Turkey. This study is within the scope of Gökberk Şerbetçi›s master's thesis.

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POSTER PRESENTATIONS

P001
SYNTHESIS AND ELUCIDATION OF SOME NEW CARBAMATE COMPOUNDS DESIGNED BASED ON THE PHARMACOPHORE GROUP OF HDAC INHIBITORS

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Introduction: Histone deacetylase (HDAC) inhibitors impact vital cellular processes like cell division, apoptosis, and differentiation, and they're under investigation for treating various diseases, including cancer, spinal muscular atrophy, Alzheimer's, diabetes, psychiatric disorders, and parasitic infections (1). Most HDAC inhibitors follow a pharmacophore model with three key components: a zinc-binding group, a surface recognition moiety, and a suitable linker group (2). Apart from FDA-approved inhibitors for cancer, many others like Entinostat (MS-275) have undergone clinical trials (3). Our study aims to synthesize and characterize some new carbamate derivatives designed using a pharmacophore model to target HDAC inhibition for anticancer activity.

Materials and Methods: After obtaining the aryl methanol derivative, transition to carbamate derivatives was achieved using 1,1'-carbonyldiimidazole (CDI). Additional binding groups were introduced by incorporating the structure of amino alkylbenzoic acid. Final products were diversified by reacting with various o-phenylenediamine derivatives. Alternatively, derivatives without expanded binding groups were obtained by reacting aryl methanol with o-phenylenediamine derivatives in the presence of CDI.

Results: 1HNMR and 13CNMR spectral data were consistent with expectations. The 1H NMR spectra of these complexes were consistent with their corresponding protons as chemical shift values and the number of hydrogens. Both the retention times and the MS spectra of the peaks in samples are evidence of the purity and the excepted structures of the synthesized compounds.

Conclusions: A Series of some novel carbamate derivatives have been synthesized successfully. Activity studies of these compounds on different cancer cell lines are under investigation.

Acknowledgements: This study is supported by TUSEB (Project No: 12220).

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P002

BIOLOGICAL EVALUATION OF ALKYLSULFONYL 1H-BENZIMIDAZOLE DERIVATIVES AS POTENTIAL ANTIBACTERIAL AND ANTIFUNGAL AGENTS

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Introduction: Benzimidazole represents a novel class of aromatic heterocyclic compounds with broad spectrum biological activities including antimicrobial function (1). This study aimed to evaluate the antimicrobial activity of a series of alkylsulfonyl 1H-benzimidazole derivatives.

Materials and Methods: The synthesis of compounds 23-36 has been reported in our previous work (2). The antibacterial activity of the compounds against five strains of Gram-positive and Gram-negative bacteria was evaluated by liquid dilution method. The compounds were also screened for antifungal activity against two Candida species using broth dilution assay based on EUCAST recommendations (3). The lowest concentration at which visible bacterial and fungal growth were inhibited was determined as the MIC values of the compounds.

Results: Compound 25 displayed broad-spectrum growth inhibitory activity against Staphylococcus aureus (ATCC 29213), methicillin-resistant Staphylococcus aureus (ATCC 43300) and Enterococcus faecalis (ATCC 29212) at MIC of 25 µg/mL, while compound 26 was showed the most potent antibacterial activity against E. faecalis (MIC; 12.5 µg/mL). Similarly, compound 26 bearing cyclohexyl and 3,4-difluorophenyl substitutions at positions 1 and 2, respectively of the benzimidazole ring also displayed the most potent antifungal activity against Candida albicans (ATCC 10231) and Candida parapsilosis (ATCC 22019) at MIC value of 16 µg/mL. Molecular docking simulation showed compound 26 binds to the studied target enzymes and displayed higher docking score in relation to the reference drugs.

Conclusions: This study demonstrated compound 26 to be the most potent antibacterial and antifungal activity and could be a promising candidate for the treatment of pathogenic microbial infections.

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P003

STUDIES ON SYNTHESIS OF NOVEL BENZYL THIAZOLYL CARBAMATE DERIVATIVE COMPOUNDS AND THEIR ACTIVITIES HDAC ENZYME INHIBITOR

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Introduction: Cancer is a multi-stage disease with the effect of genetic and epigenetic factors and accumulation of hereditary or acquired mutations in cells (1). One of the most important epigenetic rearrangements, histone acetylation is catalyzed by histone acetyltransferase (HAT) and histone deacetylase (HDAC), which function in opposition to each other (2). Studies have shown that HDAC inhibitors significantly reduce tumor growth and metastasis, do not affect all organ systems, and have toxic effects only on tumor cells (3). In this study, benzyl thiazolyl carbamate compounds were synthesized considering their HDAC inhibitory properties.

Materials and Methods: Arylmethanol was synthesized by adding sodium borohydride to 2-substituted,4-chlorothiazole-5-carbaldehyde solution. The imidazole carboxylate intermediate was obtained by mixing arylmethanol with 1,1'-carbonyldiimidazole at room temperature. Carbamate compounds are obtained by reaction of the imidazole carboxylate intermediate with substituted 1,2-phenylenediamine in the presence of trifluoroacetic acid in THF and then purified by column chromatography.

Results: The structure of the synthesized compounds was elucidated by elementary analysis, 1H NMR, 13C NMR and mass spectral data. All spectral data were in accordance with assumed structures.

Conclusions: The structures of the synthesized compounds have been elucidated and their activity studies are continued.

Acknowledgements: This study is supported by TUSEB (Project No: 12220).

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P004

STUDIES ON THE SYNTHESIS OF NOVEL IMIDAZO PYRIDINYL CARBAMATES AND THEIR HDAC ENZYME INHIBITOR ACTIVITIES

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Introduction: Cancer is a somatic disease that occurs because of the transformation of a normal cell into a tumor cell under the influence of genetic and epigenetic factors (1). The gene transcription has been dramatically affected by the epigenetic modifications in DNA. One of the epigenetic mechanisms is histone acetylation, which is controlled by two antagonist enzyme families, histone deacetylases (HDAC) and histone acetyltransferases (HAT) (2). HDACs are vital enzymes influencing how genes are expressed by changing the chromatin structure through epigenetic control. HDAC inhibitors serve as potent therapeutic agents that acetylate histones at lysine residues and promote an open chromatin conformation at tumor suppressor genes, thus inhibiting the development of tumors (3).

This study synthesized a new series of imidazo pyridinyl carbamates considering their HDAC inhibitory activities.

Materials and Methods: 1,1'-Carbonyldiimidazole (CDI) (1.80 mmol) was solved in anhydrous tetrahydrofuran (THF), the reaction mixture was cooled to 0-10 oC on ice. Imidazo pyridinyl methanol (1.00 mmol) was solved in THF, it was transferred into the reaction mixture. It was stirred at room temperature for 2 hours and then, substituted-o-phenylenediamine / substituted 2,3-diamino pyridine (2.0 mmol) and trifluoroacetic acid (1.0 mmol) was added to the reaction mixture and stirred at room temperature for 48 hours. The crude product was purified by column chromatography.

Results: The structure of the synthesized compounds was elucidated by elementary analysis, 1H NMR, 13C NMR, and mass spectral data. All spectral data were following assumed structures.

Conclusions: The structures of the synthesized compounds have been elucidated; their activity studies are continued.

Acknowledgments: This study is supported by TUSEB (Project No: 12220).

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P005

DESIGN, SYNTHESIS, MOLECULAR DOCKING AND ADME STUDIES OF NOVEL THIAZOLIDINEDIONE DERIVATIVES AS TUBULIN POLYMERASE INHIBITORS

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Introduction: Our study applied molecular hybridization to design novel anti-cancer agents, aiming to enhance efficacy by combining different active pharmacophores. These compounds are designed to selectively inhibit Tubulin Polymerization, a crucial process for cellular mitotic functions. Suppressing microtubules is believed to significantly reduce the ability of cancer cells to multiply. By using the Thiazolidinedione structure as a basis, project resulted in the development of two distinct series of novel compounds. Each series incorporated a consistent structural motif: a Thiazolidinedione nucleus which is connected to an acetophenone at position three that features different aromatic substitutions. Each series has a unique feature: the inclusion of different aldehyde groups at position five of the Thiazolidinedione scaffold. The synthesis procedure utilized trimethoxy benzaldehyde for one set and p-chlorobenzaldehyde for the second set, both of which act as structural analogues of Combretastatin A-4 and Colchicine that are aimed to act as potential tubulin destabilizing agents. Our main goal in this research was to combine the thiazolidinedione structure with biologically active components, using a synthetic approach that targeted tubulin polymerization.

Materials and Methods: The synthesis was carried out using a three-phase methodology. The core structure of thiazolidinedione was constructed by combining chloroacetic acid with thiourea and subsequent reflux. Subsequently, a combination of different acetophenones with different aromatic substitutions was introduced onto the nitrogen of thiazolidinedione structure by nucleophilic substitution. The synthetic procedure concluded with the incorporation of trimethoxy benzaldehyde and p-chlorobenzaldehyde, which were selectively introduced as potential inhibitors of microtubule polymerization. During this specific phase of synthesis, the mentioned aldehydes were combined using a solvent system consisting of glacial acetic acid and sodium acetate, following the principles of the Knoevenagel condensation mechanism. The cytotoxic potential of the compounds (PZ comp #1 – PZ comp #11) against MCF-7 breast cancer cells was determined using MTT assay. Vincristine was used as reference drug for cytotoxicity analysis. The cells were allowed to grow overnight to facilitate their adhesion and treated with three different concentrations of the drugs (5, 50 and 100 µM) for 48h. The cytotoxic effects of the synthesized compounds were compared with that of vincristine (3, 6.5 and 10 µM).

Results: Two compound series were synthesized aiming at tubulin polymerization. Structure analysis with Mass Spectrometry, H-NMR and C-NMR were performed at Ankara University Central Laboratory. Subsequent docking studies were done, and biologic activity studies were planned. At dose of 100µM, PZ compounds #1, 2 and 4 were cytotoxic to MCF-7 cells. PZ compounds #3 and 5 were found as cytotoxic between the range of 100µM-50µM. PZ compound #8 was found cytotoxic at 50µM and the other compounds #6, 7, 9, 10 and 11 were cytotoxic between the range of 50-5µM.

Conclusions: Among the synthesized compounds, the cytotoxicity analysis indicates that PZ compound #9 and 11 were the most cytotoxic ones against MCF-7 breast cancer cells with respect to vincristine. Thus as a result of this study, potential PZ compounds in different series was highlighted for further investigation.

Acknowledgements: This study was supported by a grant of TUBITAK 2209-A (1919B012210537)

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P006

DESIGN, SYNTHESIS, MOLECULAR DOCKING AND ADME STUDIES OF NOVEL THIAZOLIDINEDIONE DERIVATIVES AS CDK4/6 INHIBITORS

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Introduction: Our research aimed to develop novel anti-cancer agents targeting CDK4/6 proteins, which are crucial for cancer progression and cell cycle regulation. Using the Thiazolidinedione scaffold, we synthesized two series of compounds. Each series utilized a Thiazolidinedione ring linked at the third position to an acetophenone group with varying substitutions to study their effects on biological activity. The series differed in the aldehydes attached at the fifth position: the first used pyrrole carboxaldehyde and the second used thiophene carboxaldehyde. These modifications, chosen for their structural similarities to CDK4/6 inhibitors, were evaluated for their potential to inhibit CDK4/6. Our goal was to enhance pharmacological efficacy through this dual-targeted approach, potentially improving anti-cancer therapies.

Materials and Methods: The synthesis of the thiazolidinedione derivatives was conducted through a triphasic process. Initially, the thiazolidinedione core was synthesized by refluxing chloroacetic acid with thiourea. Subsequently, various substituted acetophenones were integrated into the thiazolidinedione framework, targeting the nitro moiety present. The final synthetic phase focused on the incorporation of pyrrole carboxaldehyde and thiophene carboxaldehyde, conceptualized as CDK4/6 inhibitors. Through a Knoevenagel condensation reaction using methanol and diethanolamine, the final compounds were synthesized. The cytotoxic potential of the ALF compounds (ALF compound #12-17) against MCF-7 breast cancer cells was determined using MTT assay. Vincristine was used as reference drug for cytotoxicity analysis. The cells were allowed to grow overnight to facilitate their adhesion and treated with three different concentrations of the compounds (5, 50 and 100 µM) for 48h. The cytotoxic effects of the synthesized compounds were compared with that of vincristine (3, 6.5 and 10 µM).

Results: Two series of compounds were synthesized, each targeting the CDK4/6 protein. Structural analysis was conducted using Mass Spectrometry, H-NMR, and C-NMR at the Ankara University Central Laboratory. Molecular docking and ADME studies were conducted, followed by planned biological activity studies. The synthesized compounds' cytotoxic effects were analyzed in the MCF-7 cell line using MTT analysis for 48h. Vincristine, which is commonly used in breast cancer therapy, was used as a reference drug and based on its cytotoxicity three different concentrations of the compounds (5, 50 and 100 µM) were selected for the synthesiszed compounds. The results indicated that all of the ALF compounds had cytotoxic effect on MCF-7 cells approximately at concentration 5 µM.

Conclusions: The cytotoxicity analysis indicates that all of the ALF compounds had cytotoxic effect on MCF-7 breast cancer cells approximately at concentration 5 µM. The cytotoxicity level of the compounds were higher than that of vincristine at 48h. Thus, these promising compound from different series will need to be further investigated.

Acknowledgements: This study was supported by a grant of TUBITAK 2209-A (1919B012211294)

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P007
NOVEL (4-CHLORO-2-((1-PHENYL-1H-TETRAZOL-5-YL)THIO)THIAZOL-5-YL)METHYL (2-AMINOPHENYL)CARBAMATES AS HDAC ENZYME INHIBITORS

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Introduction: Cancer is an abnormal cell growth that can infiltrate or expand outside of its initial location. It happens as a result of genetic and epigenetic modifications that interfere with essential biological processes such as DNA damage and repair[1]. These epigenetic modifications play a vital role in gene transcription. Histone acetylation is one of the epigenetic mechanisms that is regulated by the balance between the opposing activities of histone deacetylases (HDACs) and histone acetyltransferases (HATs)[2]. Acetylation of histones modifies the structure of chromatin and alters transcription of oncogenes [3]. HDAC inhibitors are effective treatment options that can stop the growth of tumors because of their capacity to acetylate histones at lysine residues and to induce open chromatin conformation at tumor suppressor genes[4].

In this study, carbamate derivatives were synthesized for their HDAC inhibitor potencies. The structures of the synthesized compounds have been elucidated by enstrumental analysis; their activity studies are continuing.

Materials and Methods: 1,1'-Carbonyldiimidazole (CDI) (1.80 mmol) was solved in anhydrous tetrahydrofuran (THF), and the reaction mixture was cooled to 0-10 oC on ice. (4-Chloro-2-((1-phenyl-1H-tetrazol-5-yl)thio)thiazol-5-yl)methanol) (1.00 mmol) was dissolved in THF, and it was added into the CDI solution. The reaction mixture was stirred at room temperature for 2 hours and then, substituted-o-phenylenediamine / substituted 2,3-diamino pyridine (2.0 mmol) and triethylamine (2.0 mmol) was added to the reaction mixture and stirred at room temperature for 48 hours. The crude product was purified on column chromatography.

Results: The structure of the synthesized compounds was elucidated by elementary analysis, 1H NMR, 13C NMR, and mass spectral data. All spectral data were following assumed structures.

Conclusions: The structure of the synthesized compounds was elucidated; their activity studies are continued.

Acknowledgments: This work is supported by The Scientific and Technological Research Council of Turkey (TUBITAK-Project No: 221S947)

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P009
SYNTHESIS AND ANTICANCER ACTIVITY STUDIES OF NOVEL 1,3,4-THIADIAZOLE DERIVATIVES

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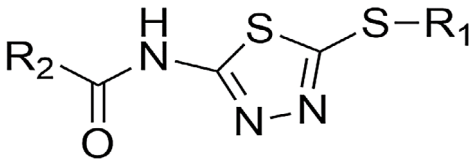
Introduction: 1,3,4-Thiadiazole ring has proven to play a significant role in pharmaceutical research area due to its diverse biological activity (1). Many studies reported that thiadiazole compounds inhibit cancer-related enzymes such as FLT3 kinase, HDAC1, VEGFR-2 and EGFR/HER-2 (2). This study aimed to synthesize new amide derivative compounds containing 1,3,4-thiadiazole ring and evaluate their antiproliferative effect.

Materials and Methods: Thiadiazole compounds were synthesized in three steps. The 5-amino-2-thiol-1,3,4-thiadiazole compound was prepared by the reaction of the starting material thiosemicarbazide and carbon disulfide in absolute ethanol (3). The thiol group of the thiadiazole compound was substituted with a small group (R1). New thiadiazole amide derivatives were obtained by reacting the amine group with suitable carboxylic acid derivative compounds (R2). The resulting compounds were purified and their chemical structures were elucidated by instrumental analysis methods such as NMR, mass and elemental analysis.



Results: In this study, some new thiadiazole-containing compounds were prepared. The anticancer activity of synthesized compounds was evaluated by MTT test in the 0.06-23 µM concentration range on the breast cancer cell line MDA-MB-468 and the human colorectal carcinoma cell line HCT-116.

Conclusions: The synthesized compounds generally showed higher cytotoxic activity on MDA-MB-468 cells. However, none of the compounds was more potent than standard nilotinib. Additionally, previous research papers reported that some 1,3,4-thiadiazole amide derivatives have exhibited EGFR inhibition. Based on this, EGFR enzyme inhibition activity of compounds synthesized in this study will be carried out using Elisa kits of EGFR enzyme.

Acknowledgement: This research was supported by Ankara University Scientific Research Projects Coordination Unit with project number TYL-2023-2960. We appreciate the support provided by Ankara University Faculty of Pharmacy Central Laboratory in acquisition of the instrumental analysis for the study.

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P010
DESIGN, SYNTHESIS, AND BIOLOGICAL EVALUATION OF AZOLE-HYDRAZONE DERIVATIVES AS POTENTIAL TYROSINASE INHIBITORS

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Introduction: Melanin is a polymer pigment that has a crucial role in the pigmentation of skin, hair, and eyes in humans. This pigment, produced in the melanocytes, also protects human skin from ultraviolet radiation damage and oxidative stress. However, abnormal level of melanin causes skin disorders such as melanoma and hyperpigmentation. Tyrosinase, a key enzyme in the regulation of melanin biosynthesis, is a copper-containing metalloenzyme. Therefore, tyrosinase inhibition is a promising strategy for the treatment of melanin-induced skin disorders [1]. Azoles, which are five-membered heterocyclic rings, are versatile pharmacophores with a wide range of biological activity profiles [2]there is now a great concern regarding the lower discovery rate of antifungal drugs in comparison to antimicrobial agents. Drugs conventionally used in clinics are not adequate enough to combat the increasing fungal infections, especially fungal forms resistant to fluconazole. Among the limited antifungal agents in clinics, azoles have the largest number of drug candidates in clinical trials and are partly marketed due to the particular focus of pharmaceutical companies and medicinal scientific centers. With the rise in the number of papers on azole antifungal design and discovery, a more in-depth understanding the most recent and authentic information about this class of drugs might be beneficial. To this end, we for the first time summarized the state-of-the-art information about azole drugs, with a specific focus on those in the pipelines of pharmaceutical companies, into four generations with regard to their structural similarity. More importantly, this review highlights information on the structure activity relationship (SAR. Molecules bearing hydrazone moiety have attracted considerable attention in medicinal chemistry due to their pharmacological importance [3]. Hence, we aimed to develop novel azole-based molecules containing hydrazone functionality as potential tyrosinase inhibitors.

Materials and Methods: The target compounds were synthesized in two steps. Firstly, nucleophilic aromatic substitution was carried out with 4-fluorobenzaldehyde and azole rings to obtain 4-azolyl benzaldehydes. Then, hydrazone functionality was obtained through the reaction of cyanoacetohydrazide and 4-azolyl benzaldehydes in the presence of an acid. These synthesized compounds were evaluated for their inhibitory activity against tyrosinase enzyme at 100 µM, using kojic acid as the standard compound.

Results: The structures of the synthesized compounds were proven by 1H-NMR, 13C-NMR, and HRMS spectral analyses. According to the enzyme inhibition results obtained, the compound carrying pyrazole as the azole ring displayed better inhibitory activity than the other tested compounds.

Conclusions: In this study, azole-hydrazone hybrid compounds were synthesized and characterized using spectral techniques. The tyrosinase inhibitory activity of the synthesized compounds was investigated. As a result, the pyrazole ring appeared to be a better option for designing azole-based tyrosinase inhibitors.

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P011

SYNTHESIS, CHARACTERIZATION AND STRUCTURE ELUCIDATION OF SOME NEW ADENINE-THIOUREA DERIVATIVES BY CONVENTIONAL AND MICROWAVE SYNTHESIS METHODS

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Introduction: Antiviral drug development studies gained speed and importance because of the COVID 19 pandemic, which affected the whole world in 2019. Some antiviral drugs that are known also contain an adenine ring (such as tenofovir, adefovir). It is possible to design new and active compounds by altering functional groups with high biological activity to molecules containing adenine ring. When considering thiourea compounds, a broad-spectrum biological activity is encountered in the literature. Therefore, keeping the adenine ring, which is likely to have antiviral effects, as a side chain, and bringing together thiourea structures with high biological activity may be a rational approach for the design of a new drug molecule. (Ronchetti et al., 2021).

Materials and Methods: Microwave synthesis method is an advantageous technique in terms of saving time and materials, reducing environmental pollution, and performing synthesis reactions in solvent-free environments comparing with conventional synthesis (Gawande et al., 2014). In our study, some new and original thiourea derivatives were synthesized by microwave and conventional methods and their structures were elucidated with by spectroscopic methods.

Results: Several attempts were made to perform thiourea synthesis from adenine and substituted isothiocyanates. Acetonitrile, tetrahydrofuran, petroleum ether, ethyl acetate, acetone, methanol, 1,4-dioxane, N-N-dimethylformamide, dichloromethane, toluene, ethanol solvent systems and time limits were used for synthesis optimization. The products were determined by LC-MS and each solvent system was discussed accordingly.

Conclusions: Microwave synthesis method will contribute to the literature by obtaining promising new compounds, especially antiviral, in terms of biological activity, as well as a more effective synthesis method in future studies.

Acknowledgements: This project was supported by TUBİTAK 2209-A 2021/1 1919B012101721 University Students Research Projects Support Program.

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P012
EVALUATION OF THE ANTIMICROBIAL ACTIVITY OF NEW CHALCONE DERIVATIVES

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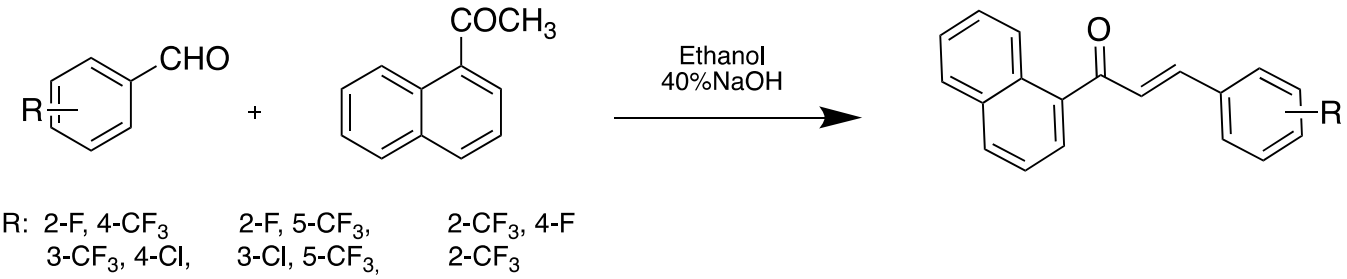
Introduction: The increase in the incidence of infectious diseases due to various reasons and the resistance to existing antibiotics in treatment increases the need for new and effective drug molecules. A significant portion of pharmaceutical research in the world is devoted to antimicrobial drug development studies. Chalcones with the main structure of 1,3-diphenylprop-2-en-1-one have been proven to have anticancer, antidiabetics, antioxidants, antimalarial, antitubercular, antiviral, anti-inflammatory, antibacterial, etc. activity1.

Materials and Methods: 1-(naphthalen-1-yl)-3-phenylprop-2-en-1-one derivatives were obtained by the reaction of aromatic aldehydes and 1-acetonaphthone according to Claisen-Schmidt reaction mechanism1.

Microbial strains: Microbial strains were obtained.The minimum inhibitory concentration (MIC) of chalcone derivatives were determined by the according to the Clinical and Laboratory Institute (CLSI)[2]. Mueller-Hinton Broth (MHB) was used as a medium to determine the minimum inhibitory concentration (MIC) value of bacterial strains.

Results: The microtiter plates, containing chalcone and test bacteria, were incubated. The last well, where no visible turbidity or growth is observed, will be considered as the minimum inhibitory concentration (MIC) for the agents3.

Conclusions: The synthesized compounds with chalcone structure have antimicrobial activity.



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3-CF_3, 4-Cl, 3-Cl, 5-CF_3, 2-CF_3

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P013

SYNTHESIS OF A GROUP OF BENZIMIDAZOLE DERIVATIVES AND IN VITRO INVESTIGATION OF THEIR *A*LPHA-GLUCOSIDASE INHIBITORY ACTIVITY

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Introduction: Diabetes mellitus (DM) poses a significant health challenge in the 21st century, with over 90% of cases being type-2 diabetes. By 2030, an estimated 643 million individuals will have diabetes, rising to 783 million by 2045 (1). Inadequately treated hyperglycemia in type-2 diabetes elevates the risk of both macrovascular and microvascular complications. Although a-glucosidase inhibitors are effective for controlling hyperglycemia, current drugs like acarbose, miglitol, and voglibose often cause gastrointestinal side effects. Thus, there's a demand for new inhibitors with higher potency, fewer side effects, and cost-effectiveness (2). Medicinal chemists are exploring heterocyclic structures, prevalent in many drugs, as potential candidates. Here, we present our study on synthesizing and assessing the inhibitory potency of four benzimidazole-acetamide derivatives (Figure 1) on the a -glucosidase enzyme.

Materials and Methods: The title compounds were prepared in a three-step synthesis. Firstly, o-phenylenediamine and acetic acid were heated to obtain the 2-methyl-1H-benzimidazole. In the second step, 2-chloroacetyl chlorides reacted with appropriately substituted anilines, yielding 2-chloroanilides. Then, these intermediates refluxed in DMF/K2CO3 to furnish title compounds EE0-EE3. The structures of the compounds were confirmed by IR, 1H NMR and ESI-MS data. The enzyme inhibition assay was carried out spectrophotometrically using a-glucosidase enzyme from Saccharomyces cerevisiae. Acarbose served as the reference compound. Calculations were done using Microsoft Excel, GraphPadPrism, and Sigma Plot.

Results: According to the biological activity results, the tested compounds exhibited a-glucosidase inhibitor activity close to or slightly better than acarbose. The most active compound in the series is compound EE-3, bearing a 4-methoxyphenyl ring on the nitrogen atom of the acetamide group, exhibiting the inhibition with an IC50 value of 1.088 ± 0.032 mM against the a-glucosidase enzyme.

Conclusions: In this study, four benzimidazole-acetamide derivatives were designed, synthesized, and evaluated for their a-glucosidase inhibitory activities. The biological activity results demonstrated that derivatives may lead to a promising anti-diabetic candidate molecule.

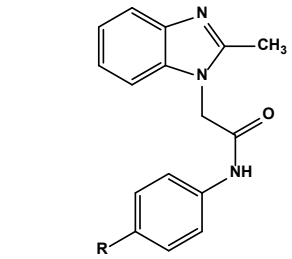

Figure 1. Chemical structure of the title compounds

Acknowledgements: This study was supported by a grant from TUBITAK 2209-A University Students Research Projects Support Program (1919B012318383).

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P014
EVALUATION OF CHOLINESTERASE INHIBITORY ACTIVITIES OF 2-AMINOPYRIMIDINE-PHENYLUREA DERIVATIVES AND MOLECULAR DOCKING STUDIES

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Introduction: Alzheimer's disease (AD) is a multifactorial disorder, which is characterized by loss in memory, degradation in language skills, behavioral abnormalities, and other cognitive impairments. The cholinergic hypothesis is one of the strategies in the treatment of AD. Based on this hypothesis, the dramatic decrease in cholinergic neurotranmission, which results from decreased levels of acetylcholine (ACh) in the brain areas, is believed to be one of the main causes of memory impairments (1). Many pyrimidine scaffolds have been showed a broad range of pharmacological activities including anti-proliferative, antiviral, antitumor, anti-inflammatory, antibacterial, antifungal, anti-β-glucuronidase, anti-Alzheimer, and antitubercular activities (2). In this work, some pyrimidine-phenylurea derivatives were evaluated as acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) inhibitory activities. In order to predict the binding interactions of the compounds with AChE/BuChE, molecular docking study was performed.

Materials and Methods: The inhibitory activities of the target compounds against AChE and BuChE in vitro were tested with Galantamin as the reference compound according to Ellman method.

Results: All compounds have more inhibitory activity on BuChE than AChE. Compound 6 [1-(2-amino-6-(4-(4-fluorophenyl)piperazin-1-yl)pyrimidin-4-yl)-3-(4-chloro-3-trifluoromethyl) phenyl)urea] exhibited better BuChE inhibitory activity with IC50 value of 11.43±0.62 µM than AChE (IC50 = 196.68±1.12 µM), which were comparable to Glantamin (IC50 = 16.58±0.18 µM) as reference compound. According to molecular docking study, compound 6 showed key interaction with the enzyme active site.

Conclusions: The above results indicated that compound 6 could be a promising molecule to obtain more active compound and investigate the mechanisms of action for AD.

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P015
INVESTIGATION OF N-(4-PYRIDINYLAMINOMETHYL)-PHTHALIMIDE AS MTDL FOR THE TREATMENT OF AD AND T2DM

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Introduction: Recently, a great deal of research has found that there is a link between AD and T2DM as they share many common pathophysiological mechanisms associated with insulin resistance, such as oxidative stress, insulin signaling impairment, mitochondrial dysfunction and neuro-inflammation. Besides, several epidemiological studies have revealed that patients with T2DM are at 1.5 times higher risk to develop cognitive impairment and dementia than individuals without diabetes (1). Lately, researchers have turned to several promising approaches including MTDLs to design and synthesize new drug candidates that can interact with multiple targets for the treatment of AD and T2DM, both possess multifactorial pathophysiology (2). Taking this into consideration, in the present study N-(4-pyridinylaminomethyl)-phthalimide derivative (Figure 1) was designed, synthesized and tested in vitro for its acetylcholinesterase (AChE), butyrlcholinesterase (BChE) and α-glucosidase inhibitory activity for the treatment of both diseases.

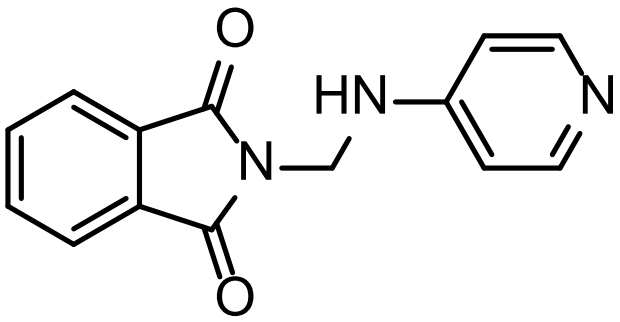

Figure 1. Structure of the synthesized compound

Materials and Methods: The synthetic approach to obtain target compound was realized in two steps (3). The structure of the title compound was verified by spectral analysis (IR, 1H-NMR and MS). In vitro determination of AChE, BChE and α-glucosidase inhibitions were performed spectrophotometrically using tacrine hydrochloride and acarbose as reference drugs, respectively (4,5).

Results: N-(4-pyridinylaminomethyl)-phthalimide derivative was synthesized and purified in the present study. According to the biological activity results, tested compound showed moderate to weak inhibitory activity in comparison to the reference drugs.

Conclusions: Our preliminary screening result might imply the usefulness of this class of phthalimide derivative to develop new MTDLs for further studies.

Acknowledgements: The authors thank to the Pharmaceutical Sciences Research Centre (FABAL) at Ege University, Faculty of Pharmacy for spectral analysis and biological studies of the compound.

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P016
INVESTIGATION OF POTENTIAL ANTIOXIDANT AND CYTOTOXIC ACTIVITIES OF NOVEL HYDROXYPYRIDINONE DERIVATIVES

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Introduction: Hydroxypyridinones (HPOs) are important nitrogen-containing heterocyclic core structures and have attracted increasing interest in drug design and discovery in recent years. These substances are promising agents for therapeutic use because of their pharmacological activities, including antioxidant, antibacterial, antifungal, anticancer, anticonvulsant, antiviral, and anti-inflammatory activities (1,2). In this study, we aimed to synthesize a novel series of HPO derivatives and evaluate their potential antioxidant and cytotoxic activities.

Materials and Methods: The compounds were synthesized by using a well-known Mannich reaction to obtain final HPO derivatives. Hydroxypyridinone core structure synthesized from kojic acid was undergone Mannich reaction with various substituted secondary amine derivatives and formaldehyde so title compund were obtained (3). The crude products were purified by crystallization from the appropriate solvents and characterized by spectroscopic methods (1H-NMR, 13C-NMR and HRMS). The antioxidant potential of these compounds was evaluated in vitro using DPPH and ABTS radical scavenging assays. In addition, cytotoxicities on MCF-7, Caco-2 and NIH-3T3 cell lines were examined by MTT assay.

Results: Among the synthesized compounds, the derivative bearing 4-fluorophenyl piperazine moiety linked to N-methyl HPO, showed 49% cell viability in MCF7 cell line. The derivative bearing 4-nitrorophenyl piperazine moiety linked to N-methyl HPO ring demonstrated 93% cell viability in the NIH-3T3 healthy cell line, thus not causing cytotoxicity in healthy cells. In addition, this compound showed significant antioxidant activity.

Conclusions: New HPO derivatives were synthesized by the Mannich reaction. The cytotoxic and antioxidant activities of the compounds were evaluated. It is thought that further studies should be continued to utilize these compounds as multifunctional agents due to their anticancer and antioxidant activities.

Acknowledgements: This study was supported by Scientific and Technological Research Council of Turkey (TUBITAK) under the Grant Number 122S035. The authors thank to TUBITAK for their supports.

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P017
SYNTHESIS AND CALCIUM CHANNEL BLOCKING ACTIVITY OF TETRAHYDROCHROMENE-3-CARBONITRILE DERIVATIVES

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Introduction: 1,4-dihydropyridines (DHPs) are one of the most important heterocyclic rings that play an important role in synthetic and medicinal chemistry, particularly for their calcium channel blocking effects (1). Hexahydroquinolines (HHQs) that contain DHP scaffold in a condensed ring system are known to have calcium channel blocking activity (2,3). In addition, tetrahydro-4H-chromene derivatives, which have a similar structure to HHQ, have been previously shown to have calcium channel blocking potential (4). In this study, we designed new potential calcium channel blockers with tetrahydrochromene structure in which the nitrogen of HHQ scaffold is replaced by oxygen. In addition, various modifications were carried out at C-4 phenyl of the tetrahydrochromene ring by using different substituents.

Materials and Methods: The synthesis of the compounds was carried out by the reaction of 4,4-dimethyl-1,3-cyclohexanedione, malononitrile, different benzaldehydes, and excess ammonium acetate in ethanol. The chemical structures of the obtained compounds were elucidated by 1H NMR and 13C NMR spectroscopy. The effects of the modifications on the L- and T-type calcium channel blocking activity of the compounds were tested using the patch-clamp method.

Results: The proposed chemical structures were confirmed by various spectral techniques and the blocking ratios of the molecules on L- and T-type calcium channels were determined.

Conclusions: The findings obtained in this study provide a different dimension to the structure-activity relationships of DHP-derived calcium channel blockers. The results are expected to guide the development of new compounds, especially for the treatment of hypertension.

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P018
EVALUATION OF SEVERAL PYRROLOPYRIMIDINE-PHENYLUREA COMPOUNDS AS RECEPTOR TYROSINE KINASE INHIBITORS

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Introduction: The arylurea scaffold has garnered interest and is frequently employed in the development of multikinase inhibitors. The current study assessed the RTK-inhibitory activities, apoptotic and cell cycle effect of several pyrrolopyrimidine-phenylurea compounds on the SW480 cell line. Additionally, quantum chemistry computations and docking studies were carried out.

Materials and Methods: RTK inhibitory activities of the target compounds were evaluated by commercial analysis kits. Cell cycle analysis was performed by Muse Cell Cycle Assay. The effects of compounds on cell apoptosis were analyzed using Muse Annexin V/Dead Cell. The docking study was performed using AutoDock vina 1.1.2. Quantum Chemistry calculations were performed using the Gaussian 03W package.

Results: Compound 3b [(1-(4-((3-chloro-4-fluorophenyl)amino)-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-2-yl)-3-(4-fluoro-3-(trifluoromethyl)phenyl) urea)] exhibited the best VEGFR-2 inhibitory activity with IC50 value of 91.02 µM. Compound 4a [1-(4-((4-chlorophenyl)amino)-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-2-yl)-3-(4-fluorophenyl)urea) has induced a significant arrest at G0/G1 phase of cell cycle ($p < 0.01$). Percentage of early apoptotic cells in compound 4a-treated SW480 cells was found as 15.14% when compared to control (4.46%). According to molecular docking study, compound 3b formed only one hydrogen bond interactions with Asp1046 by binding energy (ΔGb) of -10.7 (kcal/mole). Druglikeness properties are predicted by Molinspiration online calculation software. All of the compounds didn't obey the LogP of Lipinski's rules. Moreover, DFT calculations have been performed. Torsional angles and dipole moment of compounds have been significantly affected by the presence of the substituents. Unlike, the frontier molecular orbital energies have been little affected.

Conclusions: In order to develop more active compound, further optimization will be performed by designing the compounds with different substitutions which also obey all of Lipinski's rules.

Acknowledgements: This study was supported by a grant of TUBITAK (SBAG-214S573)

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P019
SYNTHESIS OF SOME N'-BENZYLIDENE-1H-BENZIMIDAZOLE-5-CARBOHYDRAZIDE DERIVATIVES

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Introduction: Benzimidazole ring is an essential scaffold in drug development and its derivatives as cancer therapeutics have been studied in various papers (1). Recently, N'-benzylidene benzimidazole carbohydrazides and their anticancer activities have been reported (2). In this study, we synthesized some N'-benzylidene-1H-benzimidazole-5-benzohydrazide derivatives expected to show anticancer activity.

Materials and Methods: The 1H-benzimidazole-5-carboxylic acid was prepared by the reaction of 3,4-diaminobenzoic acid and formic acid in 4N HCl solution (3). The carboxylic acid was converted to the ester compound in the presence of H2SO4 and MeOH (4). This methyl ester was treated with hydrazine hydrate to get benzimidazole-5-carboxylic acid hydrazide (2). Finally, the reaction of the hydrazide derivative with corresponding substituted benzaldehydes gave the desired products (Figure 1). 1H-NMR and 13C-NMR spectra were recorded employing a Bruker Avance Neo 500 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.

Results: Desired benzimidazole compounds were synthesized and their chemical structures were elucidated by NMR and mass spectral analysis.

Conclusions: Biological activity studies of these compounds are in progress.

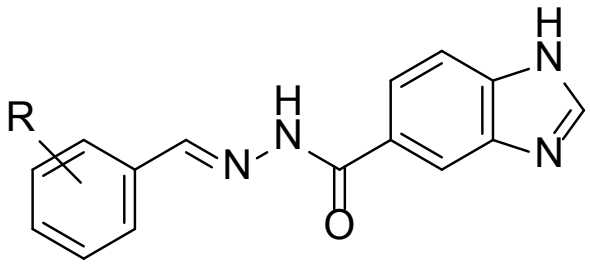

Figure 1. General formula of some N'-benzylidene-1*H*-benzimidazole-5-carbohydrazides

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P020

SYNTHESIS OF NEW 2-((5-SUBSTITUTEDBENZYLIDENE-4-OXO-4,5-DIHYDROTHIAZOL-2-YL)AMINO)THIAZOLE-4-CARBOXYLIC ACID DERIVATIVES AND EVALUATION OF THEIR ANALGESIC AND ANTI-INFLAMMATORY ACTIVITIES

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Introduction: Inflammation is the organism's response to various stimuli. Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used to treat inflammation and pain, and fever. However, as NSAIDs often have adverse gastrointestinal side effects, their use is limited. Thiazoles are heterocyclic compounds with many pharmacological activities (1,2). The analgesic, anti-inflammatory and antipyretic activities of thiazole and thiazole-4-one derivatives have been reported in many studies. In the light of this information, thiazole-4-carboxylic acid was produced, and its analgesic and anti-inflammatory activities were investigated.

Materials and Methods: Starting from ethyl bromopyruvate, thiazole-4-carboxylic acid analogs were synthesized in 4 steps. In addition, the analgesic and anti-inflammatory activities of the synthesized compounds will be investigated using the hot-plate, tail-clip, formalin, λ-carrageenan induced paw test and in silico approaches as in previous study (1).

Results: The synthesis of the compounds was carried out four steps with high yield. The structures of the compounds were clarified by NMR and HRMS techniques. In vivo and in silico results indicated that thiazole-4-carboxilic acid was useful as an antiinflammation agents and in silico studies estimated the binding mode.

Conclusions: The final molecules were synthesized highly pure and with the high yield (above 80%). Primary in vivo animal experiments have shown that the thiazole-4-carboxylic acid structure is a potential pharmacophore structure. Moreover, the contribution of the thiazol-4-one moiety to this effect was reported by in silico methods. Based on these data, the structure-activity relationship was reported.

Acknowledgements: We thank Anadolu University BIBAM and Merkez laboratory for spectroscopic analyses.

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P021
NEW SUBSTITUTED PIPERAZINE LINKED INDOLIN-2-ONES AS POTENTIAL VEGFR-2 INHIBITORS

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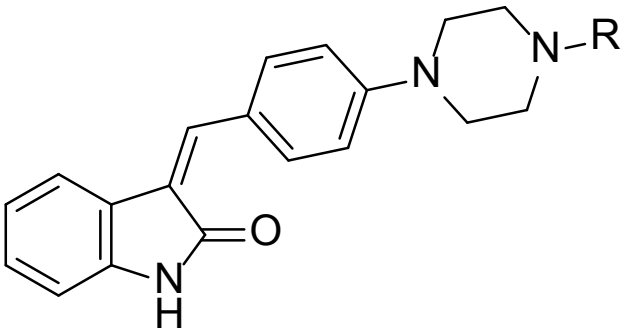
Introduction: Receptor tyrosine kinases (RTKs) are prominent targets in current anticancer drug discovery efforts due to their role in cancer pathophysiology (1). Vascular endothelial growth factor receptor-2 (VEGFR-2), a member of the RTK family, plays an important role in regulating tumor angiogenesis and the formation of new blood vessels. Studies have shown that tumor angiogenesis promotes tumor metastases and the transformation of a benign tumor into a malignant one (2, 3). In light of these findings, inhibiting VEGFR-2 signaling has been identified as a promising target for the development of new anticancer agents (4).

Materials and Methods: 4-(4-Substitutedpiperazin-1-yl)benzaldehydes were obtained by treating 4-fluorobenzaldehyde with appropriate piperazines. Subsequently, the target compounds, 3-(4-(4-substitutedpiperazin-1-yl)benzylidene)indolin-2-ones (Fig.) were synthesized by the reaction of 4-(4-substitutedpiperazin-1-yl)benzaldehydes with indol-2-one. The compounds were tested for their ability to inhibit VEGFR-2 enzyme using The BPS Bioscience® VEGFR2 Kinase Assay Kit. Sorafenib was used as a reference drug.



R= cyclohexyl, substituedphenyl

Fig.: General structure of 3-(4-(4-substitutedpiperazin-1-yl)benzylidene)indolin-2-ones

Results: In this study, novel 3-(4-(4-substitutedpiperazin-1-yl)benzylidene) indolin-2-one derivatives were designed and synthesized as potential VEGFR-2 inhibitors. The structures of the target compounds were elucidated using IR, 1H-NMR, and 13C-NMR spectral methods. Biological results revealed that the compound carrying a cyclohexyl group, by demonstrating better activity than those carrying substituted phenyl groups, was the most active derivative in the series.

Conclusions: These results can promote to design of lead compounds in the search for potent VEGFR-2 inhibitors.

Acknowledgments: This study was supported by the Scientific Research Fund Hacettepe University, Turkey (Project THD-2022-19967)

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P022
SYNTHESIS AND BIOLOGICAL ACTIVITY OF NOVEL 1,4-DIHYDROPYRIMIDINE DERIVATIVES AS POTENTIAL CALCIUM CHANNEL BLOCKERS

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Introduction: Voltage-gated calcium channels which play a critical role in the entry of calcium ions into the cells, open as a result of membrane depolarization and regulate intracellular metabolic events. Blocking calcium channels is an important therapeutic approach in the treatment of various cardiovascular and hypertensive diseases [1]. 1,4-Dihydropyrimidines (DHPs) are very important class of heterocyclic compounds that represent the most popular L-type calcium channel blockers and are widely used in the treatment of hypertension and angina pectoris [2]. Additionally, recent studies showed that DHPs can block not only the L-type calcium channel but also low-voltage activated T-type calcium channels [3]calcium channel modulators are accepted as precious molecules for the therapeutic intervention of various pathologies ranging from cardiovascular to neurological diseases. 1,4-dihydropyridines (DHPs. In the present study, we aimed to design and synthesize DHP derivatives bearing different ester or amide groups on the C-3 position of DHP as L-/T-type calcium channel blockers.

Materials and Methods: DHP derivatives were obtained by the modified Hantzsch reaction of 5,5-dimethyl-1,3-cyclohexanedione, appropriate acetoacetate or acetanilide, aromatic aldehyde, and excess ammonium acetate. The blocking ability of synthesized compounds on L- (Cav1.2) and T- (Cav3.2) type calcium channels was tested by whole-cell patch clamp assays.

Results: All compounds were characterized with 1H-NMR, 13C-NMR, and HRMS spectral analyses. The obtained biological activity results revealed that most compounds displayed a noteworthy blocking activity on Cav1.2 and Cav3.2 with different selectivity profiles.

Conclusions: The target compounds were successfully obtained according to the modified Hantzsch reaction and the ability of the compounds to block L-/T-type calcium channels were tested. As a result, the present study suggested that these compounds with ester or amide moieties could be considered potential calcium channel blockers in cardiovascular and neurological disorders.

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P023
SYNTHESIS, CHARACTERIZATION, AND CYTOTOXIC ACTIVITY OF PLATINUM(II) COMPLEXES WITH 2 AND/OR 5-SUBSTITUTED BENZIMIDAZOLE AS CARRIER LIGAND

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Introduction: Cisplatin and other platinum-based chemotherapeutic drugs have been used extensively for the treatment of numerous human cancers such as ovarian, bladder, head and neck, lung, testicular, cervical, esophageal, breast, and brain cancer (1). However, cisplatin-treated patients might encounter several problems, including the development of resistance to treatment, poor prognosis, cancer recurrence, and many adverse effects, including gastrointestinal, ototoxic, and nephrotoxic toxicities (2,3).

The benzimidazole scaffold is a heteroaromatic chemical structure that behaves as a carrier ligand in platinum complexes. This scaffold resembles the structure of purine bases and is found in vitamin B_{12} derivatives. In addition to the above-mentioned, it is also highly stable and has low toxicity, electronic, and steric properties, and its binding with metals (4).

Despite its widespread use in medical treatment, platinum-based chemotherapy drugs can cause side effects and lead to the development of resistance. Therefore, considerable effort is being made to develop new platinum-based anticancer agents with equal or higher antitumor activity but lower toxicity.

In this work, two new platinum(II) complexes were synthesized with benzimidazole that has been 5(6)-methyl-2-(1-hydroxyethyl)benzimidazole (**L**) as a carrier ligand. [Pt(**L**)$_2$Cl$_2$] (**Complex 1)** and [Pt(**L**)$_2$I$_2$] (**Complex 2)** were characterized using FT-IR and ^{1}H NMR spectra, and their cytotoxic activities were determined using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) method (5).

Materials and Methods: Complex 1 and Complex 2 were synthesized by dropwise addition of a solution of the carrier ligand in ethanol to aqueous solutions of K_2PtCl_4 or K_2PtI_4, respectively. The MTT method was tested for the cytotoxic effects of Complex 1 and 2 against MCF-7 for breast cancer, DU-145 for prostate cancer, and Ishikawa for endometrial cancer cell lines.

Results: In the present paper, two platinum(II) complexes were designed and synthesized. The chemical structures of Complexes 1 and 2 were elucidated by their FT-IR and ^{1}H NMR spectroscopic methods. In the IR spectra of synthesized complexes, prominent changes were observed. The ^{1}H NMR spectra of these complexes were consistent with their corresponding protons as chemical shift values and the number of hydrogen.

According to IC_{50} values, **Complex 1** was found to be the most active complex against the Ishikawa and DU-145 cell lines.

Conclusions: Complex 1 with chlorine-leaving groups was found to be more active than Complex 2 with iodine-leaving groups in all cell lines tested. According to MTT test results, IC_{50} values of the synthesized complexes were less effective compared to cisplatin and oxaliplatin.

Acknowledgements: This study was supported by a grant of Mersin University BAP (2023-1-TP2-4827).

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P024
SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME N-(HETEROARYLAMINOMETHYL)-BENZOXAZOLONE DERIVATIVES

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Introduction: α-Glucosidase, located on the epithelial membrane of the small intestine, is one of the pivotal enzymes which catalyzes conversion of carbohydrates to monosaccharides. With the inhibition of this enzyme, the glucose absorption from small intestine was reduced. In the light of this information, targeting α-glycosidase is emerging as an effective strategy in the treatment of type 2 diabetes mellitus (T2DM) which is one of the most challenging diseases for pharmaceutical researchers in the 21st century (1). There are many studies focused on heterocyclic scaffolds and Mannich bases which are known to exhibit many biological activities including antidiabetic acitivty (2). In this respect, in the current study, we synthesized some N-(heteroarylaminomethyl)-benzoxazolone derivatives in order to obtain new α-glycosidase inhibitors (Figure 1).

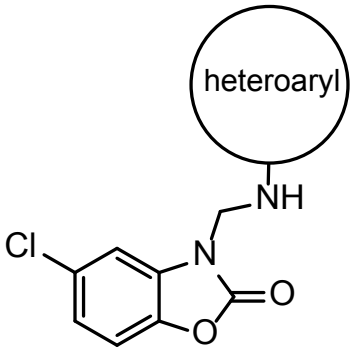

Figure 1. General structure of final compounds

Materials and Methods: The final compounds were synthesized in one-step by Mannich reaction conditions (3). Structures of the compounds were confirmed by spectral analyses (IR and 1H NMR). In vitro α-glucosidase enzyme inhibition studies were carried out spectrophotometrically in comparison to reference drug acarbose (4). In addition, enzyme inhibition kinetic assay was performed in order to understand inhibition type of the most active compound.

Results: All of the compounds obtained within the scope of our study are new, and their synthesis, spectral data, and biological activities were reported for the first time in this study. Based on biological activity results, tested compounds exhibited good to moderate α-glucosidase inhibitory activity when compared to acarbose.

Conclusions: In conclusion, our obtained results indicated that these derivatives could be considered a starting material and open new doors for the development of novel α-glycosidase inhibitors.

Acknowledgements: The authors thank to the Pharmaceutical Sciences Research Centre (FABAL) at Ege University, Faculty of Pharmacy for spectral analysis and biological studies of the compound.

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P025
SYNTHESIS AND INVESTIGATION TYROSINASE INHIBITOR ACTIVITIES OF NOVEL COMPOUNDS CARRYING 4-(4-FLUOROBENZYL)PIPERAZINE FRAGMENT

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Introduction: Tyrosinase is the key enzyme in the biosynthesis of melanin, which plays a crucial role in the pigmentation of skin, hair, and eyes. An uncontrolled increase in melanin production can cause skin problems such as blemishes, hyperpigmentation, and melasma. Tyrosinase inhibitors reduce melanin formation by inhibiting melanogenesis (1). It has been demonstrated in the literature that many compounds containing the 4-(4-fluorobenzyl)piperazine structure have tyrosinase inhibitory effects (2, 3). In this study, we aimed to design and synthesize a series of novel compounds carrying the 4-(4-fluorobenzyl)piperazine fragment capable of tyrosinase inhibition and to investigate their antityrosinase activities.

Materials and Methods: The structure of the target compounds (Figure 1) which were synthesized starting from 4-(4-fluorobenzyl)piperazine, were confirmed by spectroscopic data (FT-IR, 1H- and 13C-NMR) including X-ray studies.

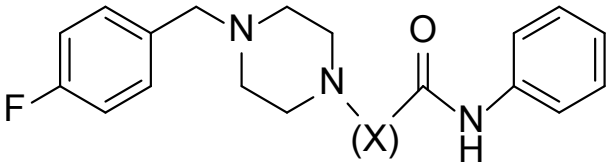

Figure 1. Structure of the target compounds

Results: Tyrosinase inhibition of synthesized compounds was evaluated against kojic acid. Some of the target compounds showed moderate tyrosinase inhibitor activity.

Conclusions: This study may lead to further development of novel compounds carrying 4-(4-fluorobenzyl)piperazine fragment, as a tyrosinase inhibitor.

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P026

DESIGN AND SYNTHESIS OF SOME NEW CHROMONE DERIVATIVES AS ADENOSINE MONOPHOSPHATE ACTIVATED PROTEIN KINASE (AMPK) ACTIVATORS

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Introduction: AMPK is a member of the protein kinase family. It is involved in the regulation of energy hemostasis by sensing the energy level in the cell (1). AMPK activation, anabolic pathways that require energy are stopped, while catabolic pathways that produce energy are activated (2). AMPK protects the cell under physiological (hypoxia, exercise) or pathological (infection, chemical carcinogenesis, ROS) stress conditions (3). It also promises hope for the treatment of diseases such as type 2 diabetes and obesity due to its effects on carbohydrate and fat metabolism, such as stimulating glucose uptake in skeletal muscle and triggering fatty acid oxidation (4,5). The first known small molecule AMPK activator has a thienopyridine ring and a biphenyl residue attached to it. The compounds planned to be synthesized in this study contain chromone ring, considering their current effects.

Materials and Methods: Before the synthesis of the designed compounds, docking studies were carried out with AutoDock Vina. Then, starting from phenol derivatives and biphenyl acetic acids, their synthesis of the chromone derivatives bearing biphenyl moiety was carried out in two steps using the Friedel Crafts acylation method (6).

Results: Structure elucidation of the synthesized compounds was carried out by 1H NMR and 13C NMR. The analysis results supported the structure that are planned to be synthesized.

Conclusions: The compounds designed as AMPK activators interacted with the desired amino acid residues and showed similar spatial structure. In the next step, the synthesized compounds will be evaluated as AMPK activators and especially for their anticancer activities.

Acknowledgements: This study was supported by a grant of TUBITAK (220S193)

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P027
DETERMINATION OF SOME INDOLE DERIVATIVES AS ACHE AND BUCHE INHIBITORS FOR ALZHEIMER'S DISEASE BY MOLECULAR DOCKING STUDIES

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Alzheimer's disease is a neurodegenerative disease characterized by cognitive decline and cholinergic system dysfunction. Acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) are enzymes involved in the breakdown of acetylcholine, a neurotransmitter critical for cognitive functions. Inhibitors targeting these enzymes are therapeutic approaches for Alzheimer's disease. In this study, we have reported the in-silico studies of novel potential active compounds by synthesizing hydrazide-hydrazon derivatives of the 5.6 dimethoxy indole compounds, isosters of the Donepezil (1) structure of indanon ring. The enzyme-receptor interactions of compounds on AChE/BuChE were studied compared to the reference compound Donapezil.

Materials and Methods: The crystal structures of the AChE/BuChE were obtained from the Protein Data bank (PDB, http://www.rcsb.org). Ligand groups optimized in Chimera and the docking study was performed in Auto Dock Vina 4.2.6 software. The XYZ coordinates were set to -14.01, -43.83, and 27.66 (2).

Results: Protein-Ligand interaction plays a significant role in structure-based drug design studies. Conformations with the lowest docked energy and RMSD value and highest hydrogen bonding capability were chosen as a strongest binding capability. Most of the compounds showed good binding capability.

Conclusions: The results indicate the possibility of the designed compounds may be biologically active due to similar interactions to donapezil.

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P028
SYNTHESIS AND BIOLOGICAL ACTIVITY STUDIES ON NOVEL THIOUREA DERIVATIVES

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Introduction: It is known that thiourea derivatives are used effectively in the pharmaceutical industry and are useful in the treatment of many diseases, by reducing or preventing their symptoms. Also, 1,3-disubstituedthiourea derivatives had been especially used as active substances in the treatment of several diseases (1,2).

Materials and Methods: The target compounds were obtained by refluxing different anthranilic acid derivatives with various isothiocyanates in dry acetone medium (2). The structures of the obtained compounds were elucidated by using different spectroscopic methods such as IR, 1H-NMR, 13C-NMR, besides elemental analysis. The inhibitory effects of the compounds against DPPH radical scavenging, α-glucosidase, and acetylcholinesterase were investigated by using spectrophotometric method (3).

Results: In this work, eight novel thiourea compounds were synthesized from different anthranilic acids. The results showed that the compounds had moderate radical scavenging activity according to gallic acid (92.25 ± 0.14% at 100 µM) which was used as a reference compound. Compound 5 in the presence of trifluoromethyl group demonstrated the highest α-glucosidase inhibitory effect with 52.26 ± 2.35% at 100 µM. On the other hand, the compounds demonstrated low AChE inhibitory effects compared to galantamine (80.33 ± 0.77% at 100 µM) which was used as a reference compound.

Conclusions: The results showed that detailed studies can be conducted on the potential of compound 5 to be used in the treatment of Diabetes Mellitus.

Acknowledgements: This study was partly supported by the TUBITAK (Scientific and Technological Research Council of Turkey). Project Name: 2209-A - Research Project Support Programme for Undergraduate Students (1919B012208013).

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P029
IN SILICO STUDIES OF SOME NOVEL METHYL BENZOXAZOLE-6-CARBOXYLATE DERIVATIVES AS HTOPO IIα INHIBITORS

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Introduction: Human DNA topoisomerase II is one of the important targets in anticancer therapy (1-3). Despite the clinical success of drugs targeting topoisomerase II, there is a need for new DNA Topo II enzyme-targeted anti-tumor drugs due to some side effects and limited clinical efficacy with the development of resistant cancer cells. The aim of this study is to in silico design some new methyl 2-(substitutedphenyl)benzoxazole-6-carboxylate derivatives that may have anticancer effects targeting the hTopo IIα enzyme.

Materials and Methods: Molecular docking and ADME/Tox calculations were performed as in silico studies by using Cresset Flare (4) to understand the interactions between designed benzoxazoles with hTopo IIα which was received from Protein Data Bank (PID: 5GWK) (5) and pharmacokinetic properties of them.

Results: According to the molecular docking study, it was found that the designed benzoxazole derivatives interacted well with the active site of the hTopo IIα enzyme, similar to the original ligand Etoposide and docked compounds were bound to enzyme with between -6,506 and -11,224 LF Rank Score. Moreover, it is predicted that all of the designed benzoxazole derivatives comply with Lipinski's rule of 5 and hence they will exhibit good pharmacokinetic properties.

Conclusions: It is concluded that these benzoxazole derivatives may be promising compounds for hTopo IIα enzyme targeted cancer therapy and should be supported by in vitro studies in the future.

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P030
SYNTHESIS AND ANTIMICROBIAL ACTIVITIES OF PLATINUM(II) COMPLEXES WITH AZOLE DERIVATIVES AS CARRIER LIGANDS

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Introduction: The discovery of cisplatin by Rosenberg revolutionized the use of metal-based compounds in medicine, especially in the treatment of cancer and microbial diseases. After this important discovery, scientists have rapidly increased their studies on these compounds with potential biological uses, indicating that the medical use of metal-based compounds is a promising topic (1). The use of biologically active compounds, such as the azole ring found in vitamin B_{12}, and purine bases, as carrier ligands is a notable approach in developing new metal complex medications (2). In this study, *in vitro* antimicrobial activities of synthesized complexes of the type $[Pt(L1)_2I_2]$ (**Complex 1**) and $[Pt(L2)_2I_2]$ (**Complex 2**) (L1= 1*H*-1,3-diazole and L2= 1*H*-benzo[d] imidazole) have been evaluated by the microdilution method.

Materials and Methods: The corresponding ligands, and K_2PtI_4 were dissolved in ethanol:water. The reaction mixture protected from light was heated at 30-40 °C for 3-6 days. The *in vitro* antimicrobial activities of **Complex 1** and **2** have been evaluated by microdilution method (3) against Gram-positive bacteria, Gram-negative bacteria, and yeast-like fungi.

Results: In the present paper, the chemical structures of **Complex 1** and **2** were elucidated by IR and ^{1}H-NMR spectroscopic methods. In the IR spectra of synthesized complexes, prominent changes were observed. The ^{1}H-NMR spectra of these complexes were consistent with their corresponding protons as chemical shift values and the number of hydrogens.

Conclusions: Synthesized complexes have been shown to have the desired purity and molecular structure. In general, **Complex 1** and **2** can be considered as promising antibacterial activity against Gram negative bacteria such as *Klebsiella pneumoniae ATCC 100031, Escherichia coli ATCC 25922, Acinetobacter baumannii ATCC 19606.*

Acknowledgements: This study was supported by a grant of Mersin University BAP (2023-1-TP2-4828)

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P031
DETERMINATION OF ANTIOXIDANT ACTIVITY OF 2-MERCAPTOSUBSTITUTED 1H-BENZO[D]IMIDAZOLE COMPOUNDS

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Introduction: 2-Mercaptosubstituted 1*H*-benzo[d]imidazole derivatives are important active molecules with pharmacological properties such as antiulcerative, antioxidant, anticonvulsant, analgesic, and antimicrobial (1). Thiol groups have significant functions such as scavenger activity, redox regulation, and metabolite transfer, which can cause them to exhibit inhibitory or accelerating effects on metabolic processes (2). Free radicals are highly reactive molecules that play a crucial role in the development of several chronic diseases. To counteract this, the body has an antioxidant system, which includes enzymatic systems and scavengers such as glutathione-GSH, ascorbate, and vitamin E (1,2). In this study, 2-SH/-CH_2SH and/or 5-H/-CH_3-substituted-1*H*-benzo[d]imidazole compounds were evaluated using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) method to investigate their potential antioxidant activity (3).

Materials and Methods: 2-mercaptomethyl-5-substituted-1*H*-benzo[d]imidazoles were synthesized by the Philips method (4). To evaluate the antioxidant activity, each sample prepared was at various concentrations, and standard ascorbic acid solutions were taken. The experiment was repeated three times, and the percentage inhibition of DPPH free radical scavenging activity and IC_{50} values were calculated with the Prism application.

Results: The chemical structures of the synthesized compounds were elucidated by melting point, and FT-IR, ^{1}H-NMR spectroscopic methods. 2-thiomethylbenzimidazole exhibited strong antioxidant activity in the DPPH assay, capturing 96% of the DPPH radicals. However, it was found to be slightly less effective compared to the reference antioxidant ascorbic acid, which showed 96.5% inhibition.

Conclusions: Our results may suggest that 2-thiomethylbenzimidazole could be a promising candidate for further investigation as an antioxidant.

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P032
VOLTAMMETRIC DETERMINATION OF TERAZOSIN HCL FROM PHARMACEUTICAL DOSAGE FORMS USING POLY(ALLURA RED AC) MODIFIED GLASSY CARBON ELECTRODE

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Introduction: Benign prostatic hyperplasia is a condition associated with age and influenced by androgens, resulting in low urinary tract syndromes such as urgency, daytime frequency, nocturia, incontinence, dysuria etc. (1,2). Terazosin HCl (TRZ) is an orally used α1-adrenergic-receptor antagonist for the treatment of low urinary tract syndromes (1). Sensitive determination of TRZ is important to minimize or avoid side effects commonly experienced during treatment, including dizziness, headache, upper respiratory tract infection, and stomach pain.

Materials and Methods: A three-electrode electrochemical cell was used for the experiments. It contained a glassy carbon (GC) electrode as working electrode, a platinum wire as counter electrode, and Ag/AgCl electrode as reference. All measurements by cyclic voltammetry (CV) and differential pulse stripping voltammetry (DPSV) were performed using a computer-controlled Autolab potentiostat/galvanostat with Nova 1.10 software (Metrohm-Autolab, The Netherlands).

Results: The GC electrode was electrochemically modified with poly(Allura Red AC) for the determination of TRZ. Electrochemical oxidation behavior of TRZ was examined using CV and DPSV techniques with the polymer modified GC electrode. TRZ exhibited an irreversible anodic peak at approximately 829 mV in Britton-Robinson buffer at pH 5.0. Analysis of scan rates suggested that the oxidation reaction of TRZ was adsorption-controlled on the polymer modified GC electrode. Operational parameters were optimized for the DPSV method, leading to a calibration plot showing linearity within the concentration range of 0.04-8 µM with a detection limit of 0.713 nM. Recovery experiments were performed using pharmaceutical dosage forms of TRZ and resulted in quantitative recovery of 100.40% with a relative standard deviation of 0.76%.

Conclusions: In conclusion, a highly sensitive, selective, and thoroughly validated DPSV method for TRZ determination was developed and effectively utilized in analyzing spiked pharmaceutical samples.

Acknowledgments: This study was funded by KTU-FBA-2018-7456.

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P033

DEVELOPMENT OF A NEW POLYMER-BASED ELECTROCHEMICAL SENSOR FOR ANALYSIS OF MELATONIN AND ITS DETERMINATION FROM PHARMACEUTICALS AND BIOLOGICAL SAMPLES

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Introduction: Melatonin (N-acetyl-5-methoxytryptamine) is the pineal hormone and synthesized from tryptophan as a precursor (1). Melatonin has various effects on biological, physiological, and neuroendocrine processes such as circadian rhythms, immunologic responses, and reproduction. It also has properties such as anti-tumor and anti-aging (2). It is also used as a medication to treat various sleep disorders and jetlag. Melatonin treatment is effective in improving sleep quality and regulating sleep/wake rhythm in these patients (3). Therefore, it is important to monitor melatonin levels in patients with sleep disorders or receiving melatonin treatment. In this study, a polymer-based modified electrode was developed for the rapid, simple, and effective determination of melatonin.

Materials and Methods: An Autolab PGSTAT128N (Metrohm) potentiostat/galvanostat was used for all voltammetric measurements and analysis results were evaluated using the NOVA 1.19 software. Experiments were carried out with an electrochemical cell consisting of a glassy carbon electrode (GCE) working electrode, an Ag/AgCl reference electrode, and a Pt wire counter electrode.

Results: Highly sensitive electrochemical methods were developed for the determination of melatonin on bromophenol blue polymer modified GCE. The optimum response was obtained in Britton-Robinson buffer at pH 8.0 by cyclic voltammetry (CV), differential pulse voltammetry (DPV), and square wave voltammetry (SWV). Calibration responses was found linear over the range of 0.2−10 µM for DPV and 0.4−10 µM for SWV with low detection limits. The developed sensor has been successfully used for melatonin determination from pharmaceuticals and biological samples with very good recoveries ranging from 99.1 to 100.3%.

Conclusions: The developed sensor exhibited excellent sensitivity, selectivity, and reproducibility and was used successfully for determination of melatonin from pharmaceuticals and biological samples.

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P034

SPECTROSCOPIC AND IN SILICO APPROACHES ON THE INTERACTION BETWEEN ORPHAN DRUG NITISINONE AND BOVINE SERUM ALBUMIN.

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Introduction: Nitisinone (NTBC), originally used as a herbicide, is now being used in the treatment of Hereditary Tyrosinemia Type I (HTT I) disease. Understanding the interaction between Nitisinone, and bovine serum albumin (BSA) is essential for understand the drug's pharmacokinetics and its potential influence on protein binding in the bloodstream. This interaction is crucial in determining the drug's distribution, effectiveness, and overall availability in the human body.

Materials and Methods: This study investigated, for the first time, the interaction between NTBC and BSA using a range of analytical and computational methods including UV-Vis spectrophotometry, steady-state fluorescence spectroscopy, 3-D fluorescence spectroscopy, molecular docking, and molecular dynamics simulations.

Results: When NTBC was added into the BSA solution, a decrease in BSA fluorescence emission intensity occurred, indicating quenching. The quenching mechanism was determined to be static, a conclusion supported by UV-Vis spectrophotometry experiments. The interaction between NTBC and BSA was investigated at three different temperatures (288 K, 298 K, and 308 K), yielding binding constants of 1.44 × 105, 5.18 × 104, and 3.02 × 104, respectively, indicating a strong binding affinity between the two. Alterations in the microenvironment surrounding tryptophan (Trp) and tyrosine (Tyr) residues of BSA were observed using 3-D fluorescence spectroscopy. Thermodynamic analysis yielded values of $\Delta H = -54.34$ kJ mol−1 and $\Delta S = -0.0908$ kJ mol−1 K−1, suggesting involvement of van der Waals forces and hydrogen bonds in the NTBC-BSA interaction. Additionally, negative ΔG values across all temperatures indicated the spontaneity of the interaction. In silico investigations revealed a complex network of hydrophobic and hydrogen bond interactions between NTBC and BSA, corroborating experimental findings.

Conclusions: This study represents for the first time exploration of the interaction between NTBC and BSA, employing UV-Vis spectrophotometry, fluorescence spectroscopy, 3-D fluorescence spectroscopy, and in silico methodologies. The findings reveal a strong interaction between Nitisinone and BSA, characterized by the involvement of hydrogen bonds and hydrophobic interactions.

Acknowledgements: Mehmetcan BİLKAY thanks The Scientific and Technological Research Council of Turkey (TUBITAK) for financial support under the BIDEB/2211-A doctoral scholarship program. Şule YAZICI thanks The Scientific and Technological Research Council of Turkey (TUBITAK) for financial support under the 2209-A University Student Research Projects Support Program. İsmail Celik thanks TUBITAK ULAKBIM in Türkiye, High Performance and Grid Computing Center (TRUBA resources).

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P035
THE INTERACTION STUDY OF ABIRATERONE ACETATE AND DNA USING PHENYLALANINE-COATED COPPER NANOCLUSTERS AS A FLUORESCENT PROBE

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Introduction: Abiraterone acetate (ATA) is an FDA-approved prodrug that exerts its effects by irreversibly inhibiting the enzymatic activities of 17α-hydroxylase and C17,20-lyase, which are responsible for testosterone production, particularly. The study of drug-DNA interactions is crucial for the development of new drugs and for understanding the pharmacodynamics and pharmacokinetics of drugs. Various methods are employed to study the interaction between the drug and DNA. In this method, phenylalanine-coated copper nanoclusters were employed as a fluorescent probe to understand the interaction between DNA and ATA.

Materials and Methods: In this research, copper nanoclusters (CuNCs) were utilized as a fluorescent probe for the first time to explore interactions between drugs and DNA. Furthermore, a novel synthesis approach was developed for coating copper nanoclusters with phenylalanine (Phe). Ascorbic acid was employed as the reducing agent, while phenylalanine served as both a surface functionalizing and stabilizing agent. Characterization of Phe/CuNCs was carried out using several techniques including transmission electron microscopy (TEM), dynamic light scattering (DLS), X-ray photoelectron spectroscopy (XPS), UV-Vis spectroscopy, and fluorescence spectroscopy. Optimization studies were conducted for synthesis parameters such as ascorbic acid concentration, phenylalanine concentration, incubation time, and incubation temperature. This novel synthesis method presents several advantages including ease of synthesis, short synthesis duration, and adherence to green chemistry principles.

Results: Phe/CuNCs were employed as a fluorescent probe for studying ATA-DNA interactions. The binding constant (Kb) between ATA and DNA was determined to be 1.03 × 104. Additionally, thermodynamic analyses suggested that Van der Waals and hydrogen bonding are the predominant forces driving the ATA-DNA interaction.

Conclusions: For the first time in the literature, Phe/CuNCs were successfully utilized as fluorescence probes to investigate drug-DNA interactions. The binding constant between ATA and DNA was found to be 1.03 × 104. Additionally, thermodynamic studies demonstrated that the interactions between ATA and DNA involve hydrogen bonding and Van der Waals interactions. The newly synthesized Phe/CuNCs are noteworthy due to their rapid synthesis times, ease of preparation, high fluorescence intensity, and compatibility with green chemistry synthesis procedures.

Acknowledgements: The authors gratefully acknowledge the financial support provided by Gazi University (BAP TDK-2022-7741).

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P037
DEVELOPMENT OF A STABILITY-INDICATING RP-HPLC METHOD FOR THE DETERMINATION OF BARICITINIB IN BULK

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Introduction: Baricitinib (BAR) is a Janus kinase 1 and 2 (JAK 1/2) inhibitor that can be used for the treatment of rheumatoid arthritis, COVID-19 and alopecia areata (1). Studies related its degradation products under stress conditions are limited. The aim of this study was to develop a RP-HPLC method and forced degradation studies for the determination of BAR.

Materials and Methods: The chromatographic separation was achieved using Cosmosil C18 column (4.6 x 250 mm, 5 µm) in isocratic mode with a mobile phase consisting of 10 mM ammonium acetate and acetonitrile (70:30, % v/v) with a flow rate of 1.2 mL/min. The HPLC system is equipped with a UV detector and a fluorescence detector. The UV detector was set at 225 nm. The excitation and emission wavelengths of fluorescence detection are set at 224 nm and 414 nm, respectively. BAR was subjected to forced degradation studies by hydrolysis (acidic, alkaline), oxidation, photolysis and thermal stress. Furthermore, the stability of BAR was investigated under various conditions, including short-term and autosampler.

Results: A simple, specific, rapid, and sensitive HPLC method has been developed for quantitative analysis of BAR. BAR was found stable under photolysis, acid, thermal and oxidative hydrolysis stress conditions. However, it showed degradation under base stress conditions. A baseline separation from degradation products was achieved in all stress conditions. The stability test outcomes indicated that BAR remained stable for a minimum of 24 hours at room temperature and 6 hours in the autosampler, respectively.

Conclusions: The quality of pharmaceutical products is critical for patient safety. The degradation of active pharmaceutical ingredients can impact efficacy and safety. In the present work, rapid, specific and reproducible RP-HPLC methods have been developed for the determination of BAR in the presence of its stressed degradation products.

Acknowledgements: Betul Gur and E. Damla Gök Topak is supported by TUBİTAK 2211-A grant.

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P038

QUICK OVERVIEW ON [18F]-FDG AND OPTIMIZATION OF THE [18F]-FDG PRODUCTION PROCESS AND PRODUCTION EFFICIENCY

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Introduction: 18F-FDG is a radiotracer, a radiopharmaceutical, used in the medical imaging modality positron emission tomography (PET). 18F-FDG is now the standard radiotracer used for PET neuroimaging and cancer patient management. (1)

The scope of this study includes the optimization of the ^{18}F activity, and various other factors during and after the bombardment process in the cyclotron to ensure the highest product activity when applied to cancer patients, and reduced production and maintenance costs.

Materials and Methods: For the statistical steps, Microsoft Office Excell and Minitab 21 have been used. Through correlation tests and PCA, using the results of several hundred 18F-FDG production runs it has been determined which variables have an impact on 18F activity and production yield. Followed by a regression model rendering a set of theoretical yield and activity formulas have been obtained.

Results: Statistical results have been noted and set ready for practical test productions in the company's facility in Ankara. Results show that alterations in mechanical aspects during production give no control over the overall production yield of 18F-FDG. On the other hand, effects on the 18F-activity and Target-S rates show great responses.

Conclusions: The final test results still must be obtained but the statistical analysis and test are more than promising.

Acknowledgments: This study is supported by the Turkish Scientific and Technological Research (TÜBİTAK) under 2244 Industrial Ph.D. Fellowship Program (Project No: 118C118) with Ankara University and Eczacıbaşı-Monrol Nükleer Ürünler San. ve Tic. A.Ş

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P039
THE IMPACT OF MOTILIN'S SURFACE ADSORPTION BEHAVIOR ON ANALYTICAL SENSITIVITY

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Introduction: The gastrointestinal hormone motilin, is generated to regulate the interdigestive motility of the stomach and small intestine (1). Analytical methods that enable sensitive quantification of this peptide are required to further understand this peptide's function and discover new therapeutic targets. However, measuring peptides can be challenging due to the well-known phenomena of their non-specific binding to material surfaces (2,3). In order to improve the sensitivity and accuracy of the analytical procedures, the surface adsorption behavior of motilin on the commonly used containers was examined in this study.

Materials and Methods: The adsorption behavior of motilin on the glass, polypropylene and low-adsorption polypropylene was investigated using a recently developed HPLC-UV method. It was also examined how additives like salt, surfactant, and protein affected the peptide loss. A simple and affordable sample preparation protocol for motilin was developed based on the results.

Results: Motilin bonded to both polypropylene and glass surfaces at a high rate. The addition of salt, surfactant, and protein reduced the adsorption of motilin, but only the surfactant offered high recoveries that were near 100% and more consistent results.

Conclusions: This study highlights the significance of taking into account the adsorption properties of peptides and also provides a quick, affordable and precise sample preparation method for researchers working with motilin.

Acknowledgements: This study was supported by Research Council of Anadolu University for the support of the project (Project no. 2207S101).

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P040
CONSTRUCTION OF TIO2-CNF INCORPORATED BIMETALLIC AU-PDNPS BASED APTASENSOR FOR HIGHLY SENSITIVE FOOD ALLERGEN DETECTION IN REAL FOOD SAMPLES

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Introduction: Allergy is defined as a hypersensitivity reaction initiated by proven or strongly suspected immunological mechanisms (1). Food-induced allergic reactions are often responsible for symptoms involving the respiratory system, gastrointestinal tract, and skin (2). Peanuts used worldwide as a processed food source, pose a particularly serious problem due to the allergenic symptoms that occur. The most common peanut allergen is Arachis hypogaea (Arah1) (3) which is considered one of the most serious, life-threatening food sensitivities (4). Therefore, it is essential to develop easy-to-use, rapid and accurate analytical method to sensitively detect Arah1 allergen from food products. Herein, a selective label-free voltammetric Arah1 aptasensor based on a nanostructured screen-printed graphite electrode (SPE).

Materials and Methods: All electrochemical measurements were performed using a Palmsens4 potentiostat/galvanostat electrochemical analyser with SPE electrode and PTrace 5 version 5.9 software (Houten, Netherlands). For the preparation of label-free aptasensor, firstly the SPE surface was coated with 10 µL of TiO2-CNF (2:1) solution. Then Au-PdNPs were electrodeposited on the surface of SPE/TiO2-CNF. Arah1 aptamer (5) was immobilized on the electrode and denoted as SPE/TiO2-CNF/Au-PdNPs/Apt.

Results: The electrochemical behaviours of each modified electrode were examined by CV, DPV, and EIS in 0.1 M KCl solution containing 5 mM ferro/ferricyanide ([Fe(CN)6]3−/4-). CV results showed that both anodic and cathodic peak currents increased after each modification and the highest response was observed at SPE/TiO2-CNF/Au-PdNPs. After aptamer modification, the peak currents decreased gradually showing that the aptamer blocked the surface and prevented electron transfer. Various experimental parameters of the realized aptamer-based label-free nanostructured sensor were studied and optimized using optical and electrochemical techniques.

Conclusions: In summary using a label-free voltammetric SPE/TiO2-CNF/Au-PdNPs/Apt, very low (pg/mL) detection limit was achieved. The reliability of the aptasensor was investigated in bread and peanut butter samples with high recovery values.

Acknowledgements: This work was supported by Ankara University Scientific Research Projects Coordination Unit (Project No: FBA-2022-2628, ADEP).

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P041
PAPER-BASED DNA EXTRACTION METHOD FOR MOLECULAR DETECTION OF PATHOGEN BACTERIA

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Introduction: DNA extraction is one of the most important steps for pathogen detection using molecular techniques. The DNA obtained needs to be in high concentration and purity. The main methods used for DNA extraction include the boiling method, column extraction, and purification techniques using magnetic beads. Most existing techniques consist of three main steps: cell lysis, removal of DNA from the cell, and separation of DNA from cell debris (1,2). While classical methods have many advantages, they also have disadvantages such as the need for complex devices, high volumes of analyte, and the involvement of complex procedures. In this study, a paper-based DNA extraction method from a sample volume of 10 µL has been developed for the detection of pathogenic bacteria using molecular methods.

Materials and Methods: Glass fibers were cut into strips, fixed onto acetate surfaces, and pre-treated to bind DNA. The lysate of bacteria, which had undergone lysis and interacted with proteinase K solution, was dropped onto the strips, and washing procedures were carried out. After washing with ethanol, the DNA bound on the strips was eluted with the buffer. The obtained DNA was evaluated using a Nanodrop UV absorbance spectrophotometer and qPCR measurements.

Results: The method using the paper-based DNA extraction method was completed in a much shorter time compared to the extraction method using a spin column. The method eliminated the need for complex devices such as a centrifuge and an incubator. The detection limit of S. aureus bacteria in the qPCR was determined to be 10 cfu/mL. The characterization of DNA adhered to the surface of the glass fibers was performed using the SEM imaging technique.

Conclusion: In this study, an effective and rapid paper-based DNA extraction technique has been developed, allowing for the acquisition of pure DNA.

Acknowledgments: The authors acknowledge The Scientific and Technological Research Council of Turkey (TUBITAK) (project no: 221Z056).

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P042
DEVELOPMENT OF HPLC METHOD FOR DETERMINATION OF TEICOPLANIN FROM POLYMERIC BASED DRUG DELIVERY SYSTEM

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Introduction: Teicoplanin (TPN) is a glycopeptide antibiotic and its extended half-life facilitates convenient once-daily dosing, enhancing patient adherence to treatment regimens. As a safe and effective option for patients with penicillin allergies, it demonstrates efficacy against a wide array of gram-positive bacteria [1]. The chromatographic methods for the analysis of TPN have shown a long retention time. This study aimed to develop rapid and stability-indicating analytical method for quantifying TPN concentration using HPLC-UV and to investigate the efficiency of a polymeric-based drug delivery system.

Materials and Methods: A novel HPLC-UV methodology was developed using a Kinetex C18 analytical column (Phenomenex, USA), (150 mm×4.6 mm i.d., 5 µm) with a 1 mL/min flow rate of water containing 0.1% orthophosphoric acid and acetonitrile (75:25, v/v), the column oven is set to 35°C and detection wavelength was 202 nm. The injection volume was 10 µL.

Results: The method was validated according to selectivity, linearity, LOD, LOQ, precision, and accuracy criteria specified in the International Council for Harmonisation guidelines. It was found linear in the concentration range of 0.5-100 µg/mL for both analytes with correlation coefficient (R2) values greater than 0.999. The precision for TPN was below 5.03%. The limits of detection (LOD) and quantification (LOQ) were established using signal-to-noise ratios. The LOD was found to be 0.2 µg/mL. The LOQ, defined as the lowest concentration of the analyte with an accuracy within -2.39% and precision less than 5%, was determined to be 0.5 µg/mL.

Conclusions: In the initial trials with the drug carrier systems, the feasibility of TPN analysis with heightened selectivity was elucidated. Relative to the HPLC UV techniques in literature, it confers advantages owing to its expedited analysis time. As a result of the analytical method validation studies, the optimized method is suitable for routine analysis of TPN.

Acknowledgements: This study was supported by a grant of Ankara University Scientific Research Projects Coordination Office (21B0237008).

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P043
QUANTITATIVE ANALYSIS OF MONOMER RELEASE FROM PEDIATRIC RESTORATIVE MATERIAL DUST USING HPLC-UV

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Introduction: Common restorative materials in pediatric dentistry include glass ionomer-based restorations, compomers, and composites. The finishing and polishing procedures performed in the final stage after the restorations are completed are necessary for both the occlusal adjustment of the restoration and for creating smoother surfaces to reduce bacterial accumulation, thereby preventing the formation of secondary caries. However, during the finishing and polishing procedures of restorative materials, dust particles of a size that can penetrate deep into the lungs are produced. The elution of monomers from dust particles influences the biocompatibility of restorations. Therefore, the purpose of the present study was to investigate the elution of monomers 2-hydroxyethyl methacrylate (HEMA), triethylene glycol dimeth-acrylate (TEGDMA), urethane dimethacrylate (UDMA), from three different light-cured pediatric dental material.

Materials and Methods: In the course of our investigation, we utilized the Agilent 1100 model HPLC-UV system. Analytical separation of monomers was conducted using a Kinetex C18analytical column integrated into the HPLC system. The chosen mobile phase for the analysis comprised an ACN:H2O (10:90, v/v) mixture. Employing a gradient flow method during the analysis, the water composition, initially established at 90%, gradually reduced to 10% by the fifteenth minute. Subsequently, it was reverted to the initial ratio by the twentieth minute. The column thermostat was set at 35°C, and a detector wavelength of 210 nm, corresponding to the maximum absorbance of the substances, was selected. The injection volume employed was 5 µL. The concentration of the monomers were assessed through the application of linear regression analysis on the results derived from the calibration curve.

Results: The amount of HEMA released from the light cure glass ionomer was significantly higher than released from the conventional composite and compomer. It has been observed that all three tested monomers are released only from the compomer. The present study showed that all tested materials released different levels of tested monomers.

Conclusions: With the developed and validated method, the release and quantification of monomers from restorative materials have been successfully detected and determined.

Acknowledgements: This research was funded by TUBITAK Scientific Research Projects. Project Number: 121S933

P044
EVALUATION OF TICAGRELOR CRUSHED TABLET SUSPENSION WITH NASOGASTRIC TUBE APPLICATION BY IN VITRO ANALYSIS

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Introduction: Ticagrelor, an antiplatelet medicine, plays a crucial role in preventing blood clots. In clinical scenarios where patients cannot swallow intact tablets, administration via nasogastric tube (NGT) as a crushed tablet suspension is necessary. However, the choice of nasogastric tube can influence drug effectiveness. This study aims to evaluate the impact of different types and dimensions of nasogastric tubes on the chemical and physical effectiveness of ticagrelor crushed tablet suspension.

Materials and Methods: This study aims to evaluate the impact of different types and dimensions of nasogastric tubes on the chemical and physical effectiveness of ticagrelor crushed tablet suspension. To be able to achieve this goal, sedimentation volume analysis, particle distribution analysis, assay, dissolution, and impurity analysis were performed on both Ticasa 60 mg Film Coated Tablets and Brilique 60 mg Film coated tablets with proper device selection. According to the EMA's Q&A on the administration of oral immediate-release medicinal products through enteral feeding tubes, the largest tablets were examined, and as a sample preparation medium, half a glass of water (100 ml) was selected. To be able to see the effects of different types of nasogastric tubes, 16 Fr PVC, 16 Fr Silicon, and 16 Fr Polyurethane tubes were used. Also, to be able to see the effect of the dimensions of the nasogastric tubes, 5 Fr Silicon and 8 Fr Silicon tubes were used.

Results: Effects of different types and dimensions of the nasogastric tubes examined in this study were compared between Ticasa 60 mg Film Coated Tablets and Brilique 60 mg Film coated tablets. Ticasa 60 mg Film Coated Tablets and Brilique 60 mg Film coated tablets chemical and physical profiles were found to be similar regardless of the dimension and material of the nasogastric tube.

Conclusions: A comparison study between Ticasa 60 mg Film Coated Tablets and Brilique 60 mg Film coated tablets showed that both drug products behaved similarly in cases of different types and dimensions of nasogastric tube usage. Different types of nasogastric tube usage (silicon, PVC, and polyurethane) and different dimensions of nasogastric tubes (5 Fr, 8 Fr, and 16 Fr) gave similar sedimentation volume profile, particle size distribution, assay, dissolution, and impurity results.

Acknowledgements: This study was conducted at Nobel Pharmaceuticals.

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2. EMA's Q&A on Administration of oral immediate release medicinal products through enteral feeding tubes.

P045

SENSITIVE LIQUID CHROMATOGRAPHY/TANDEM MASS SPECTROMETRY METHOD FOR THE DETERMINATION OF ANTIDEPRESSANT DRUG VORTIOXETINE IN RAT BRAIN TISSUE

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Introduction: Vortioxetine (VOR) is an antidepressant drug with multimodal mechanism of action; it effects both in depression-related and cognitive symptoms (1). The aim of this study was to develop a sensitive and validated bioanalytical LC-MS/MS method for analysis of VOR in rat brain tissue.

Materials and Methods: Chromatographic analyses were performed in isocratic mode, and citalopram (CT) was found as a suitable internal standard. Supelco Ascentis® Express Phenyl-Hexyl column was used as stationary phase, and the mobile phase was %0.15 formic acid in acetonitrile:water (55:45, v/v). For the sample preparation to each whole brain tissue, deionized water was added (1:4, w/v). To precipitate proteins, acetonitrile was added to homogenate and the mixture was vortexed for 3 min followed by centrifugation step. The supernatant was used in preparation of study and quality control (QC) samples. A Box-Behnken Design (BBD) - based method optimization was applied to explore the impact of analytical conditions on chromatographic separation of VOR and CT. Detection was realized via a triple quadrupole LC-MS/MS system; the mass transition ion-pair has been followed as m/z 299.05→149.90 for VOR, m/z 325.20→109.05 for CT.

Results: Analytical method validation was performed according to ICH guideline M10 on bioanalytical method validation (2). The calibration curve was within the range of 30 to 450.0 ng/mL. The LOD and LOQ were performed at 10 and 30 ng/mL, respectively. Recovery was 90% for the lowest calibration standard (LLOQ) and between 98% to 105% for the other concentration levels. Retention times of CT and VOR were 2.5 and 3.5 min, respectively, and a good chromatographic separation was obtained under optimal conditions.

Conclusions: A new LC-MS/MS approach for determination of vortioxetine was successfully developed and validated. The method possesses sufficient sensitivity for the quantitative detection of VOR in rat brain tissue.

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P046

DEVELOPMENT OF A MOLECULARLY IMPRINTED POLYMER-BASED ELECTROCHEMICAL SENSOR FOR SELECTIVE AND SENSITIVE DETERMINATION OF LINCOMYCIN

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Introduction: Lincomycin (LIN) is one of the lincosamide antibiotics which is used as a bacteriostatic agents and inhibits protein synthesis [1]. In this study, a highly sensitive electrochemical sensor was designed first to detect LIN using the molecular imprinted polymer (MIP) method. A MIP-based electrochemical sensor was developed using the electro polymerization method on the glassy carbon electrode (GCE) surface. LIN showed high sensitivity and selectivity towards the template molecule in the designed sensor.

Materials and Methods: Surface and morphological characterizations of the MIP-based electrochemical sensor were carried out using cyclic voltammetry (CV), electrochemical impedance spectroscopy (EIS), scanning electron microscopy (SEM), and energy dispersive X-ray spectrometry (EDX). The differential pulse voltammetry (DPV) technique was successfully applied with high sensitivity and accuracy in the determination of LIN in standard solution, milk sample, and various fruit juices using 5 mM $[Fe(CN)_6]^{3-/4-}$ as a redox probe.

Results: After optimization experiments, the calibration range was found to be between 1 pM and 10 pM, and very low limit of detection (LOD) and limit of quantification (LOQ) were calculated. Recovery studies in milk and fruit juices have proven the sensor's accuracy. Additionally, the sensor's selectivity was evaluated using common interfering substances.

Conclusions: The results showed that the MIP-based sensor can specifically recognize LIN compared to structurally related drugs and can be reliably applied to directly determining LIN from real samples.

Acknowledgements: The authors would like to thank the support of the grant of Ankara University (Scientific Research Projects Unit) under TDK-2024-3412 project.

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P047
THERAPEUTIC DRUG MONITORING OF THE ANTIPSYCHOTIC DRUG IN PLASMA BY GC-MS

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Introduction: Schizophrenia is a serious mental illness with a lifetime prevalence of approximately 0.4% worldwide (1). Antipsychotics are the primary treatment option for patients with schizophrenia. Although 70% of patients require long-term medication to control their symptoms, at least 20% do not achieve a significant response from monotherapy with antipsychotics (2). Therapeutic drug monitoring helps dose adjustment, minimizes the risk of toxicity, and ensures cost-effectiveness in the treatment of psychiatric disorders (3). Therefore, in this study, a GC-MS method was developed for the determination of quetiapine, aripiprazole, paliparidone, and clozapine, which are antipsychotic agents, in plasma.

Materials and Methods: The antipsychotic drugs were extracted from plasma using the salt-assisted liquid–liquid microextraction technique. The method has been validated by the European Medicines Agency (EMA) Bioanalytical Method Validation Guidelines (4).

Results: The calibration curve was validated between 600-1000 ng/mL for clozapine, 100-1000 ng/mL for quetiapine, 1000-1000 ng/mL for aripiprazole, 20-120 ng/mL for paliparidone with correlation coefficients >0.99.

Conclusions: The developed method was employed for therapeutic drug monitoring of antipsychotic drug in real patient plasma.

Acknowledgements: This study was funded by Scientific Research Projects Coordination Unit of Istanbul University. Project number: 39477.

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P048

DESIGNING A GOLD NANOCLUSTERS-SUPPORTED MOLECULARLY IMPRINTED POLYMER-BASED ELECTROCHEMICAL SENSOR FOR SPECIFIC RECOGNITION AND DETERMINATION OF SCOPOLAMINE

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Introduction: Scopolamine has been used as an incapacitating narcotic in sexual crimes and robberies for decades (1). *Hyoscyamus niger, Datura stramonium, Atropa belladonna, Mandragora officinarum,* and other plants in the Solanaceae family are the primary sources of tropane alkaloids like scopolamine (SCA) (2). In this study, we developed a nanomaterial-supported molecular imprinted polymer (MIP)-based sensor for SCA.

Materials and Methods: Copper nanoclusters (CuNCs), gold nanoclusters (AuNCs), and silver nanoclusters (AgNCs) were synthesized, and tested in the sensor. These nanoclusters improved the glassy carbon electrode's (GCE) porosity and effective surface area. Moreover, the MIP structure was prepared using SCA as the template molecule, 2-acrylamido-2-methylpropane sulfonic acid (AMPS) as the functional monomer, and other components with the photopolymerization (PP) method. To improve the efficiency of the MIP-based electrode in SCA measurement, various factors, including nanomaterial effect, monomer: template ratio, dropping volume, polymerization time, extraction time, extraction solutions, and rebinding time, were carefully optimized. Detailed characterizations of the developed AuNCs/AMPS/MIP-GCE sensor and AuNCs were performed using Fourier transform infrared spectroscopy (FTIR), cyclic voltammetry (CV), and electrochemical impedance spectroscopy (EIS).

Results: AuNCs were the more sensitive nanoclusters, and they were used for further experiments. The MIP-based sensor resulted from a detailed optimization phase and gave a linear response in the 2.5 × 10–12 – 1.75 × 10– 11 M range in standard solution and spiked serum samples. The detection limit was 1.59 × 10– 13 M. The recovery experiments demonstrate the sensor's sensitivity, accuracy, and applicability. The selectivity of the designed nanomaterial-supported MIP-based sensor was calculated in the presence of 1000-fold hyoscine butyl bromide and atropine.

Conclusions: In conclusion, the developed sensors performed excellent reproducibility, repeatability, high sensitivity, and selectivity against the SCA molecule. The developed MIP-based electrochemical sensor can accurately quantify SCA in serum samples.

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P049

DEVELOPMENT AND VALIDATION OF A RAPID RESOLUTION LIQUID CHROMATOGRAPHY-DIODE ARRAY DETECTOR METHOD FOR THE DETERMINATION OF DEXKETOPROFEN AND THIOCOLCHICOSIDE

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Introduction: Dexketoprofen (DEX) is an active ingredient with anti-inflammatory effect, Its' chemical name is 2-Amino-2-(hydroxymethyl)-1,3-propanediol(S)-3-benzoylalfa methylbenzeneacetate. Thiocolchicoside (TIO) has a muscle relaxant effect. It shows a selective affinity for GABA and glycinergic receptors. Its chemical name is N-[(7S)-3-(beta-D-glucopyranosyloxy)-1,2-dimethoxy-10-(methylsulfanyl)-9-oxo-5,6,7,9 tetrahydrobenzo[a] heptalen-7 -yl] acetamide. In this study a rapid, sensitive and specific liquid chromatographic (RRLC) method was developed, validated and applied to pharmaceutical preparations of DEX and TIO.

Materials and Methods: The instrument was Agilent Technologies 1260 LC series with DAD detection. All chemical solutions were analytical grade. DEX and TIO was dissolved in mobile phase. Separation was achieved by a C18 column (4.6×100.0 mm, 3.5 µm i.d.). 25 mM phosphate buffer: acetonitrile (3:7, v/v) (pH 3.3) system was used as a mobile phase at a flow rate of 0.7 mL/min. The optimum wavelength for separation was determined as 254 nm.

Results: For the optimization of method, buffer concentration, organic solvent ratio, pH, flow rate and injection volume were investigated. Retention times for TIO and DEX were 1.206 min 2.077 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 for DEX and TIO 2.02×10-8 M and 3.07×10-8 M. The developed method was successfully applied to tablets of DEX and TIO.

Conclusions: The method described here is simple, fast, sensitive and reproducible. It was applied to tablets containing 25 mg DEX and 8 mg TIO. This method is proposed for the routine analysis of DEX and TIO.

Acknowledgements: This study was supported by a grant of BAP (TSA-2023-37231)

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P050
THERAPEUTIC DRUG MONITORING OF THE FREE AND TOTAL CONCENTRATION OF PALBOCICLIB IN PLASMA BY LC-MS/MS

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Introduction: Breast cancer affects millions of women worldwide each year. It is the most common type of cancer in women and the leading cause of cancer-related deaths. The discovery of CDK4/6 inhibitors and their demonstrated survival benefits is one of the most significant advancements in the treatment of metastatic breast cancer in the past 50 years [1].

The U.S. Food and Drug Administration (FDA) approved the first CDK4/6 inhibitor, palbociclib, in combination with letrozol as a first-line treatment for patients with ER-positive, HER2-negative advanced or metastatic breast cancer. Currently, three selective CDK4/6 inhibitors, palbociclib, ribociclib, and abemaciclib, have been approved by the FDA in the United States [2].

Materials and Methods: The unbound fraction of palbociclib in human plasma increases as hepatic function worsens. Its use may be limited due to potential hepatotoxicity, and it exhibits high plasma protein binding (approximately 85%). Palbociclib was extracted from plasma using protein precipitation, while free palbociclib was extracted using the ultrafiltration method. The test method has been validated in accordance with the European Medicines Agency (EMA) Bioanalytical Method Validation Guidelines [3]. The aim of this study was to develop an LC-MS/MS method for the therapeutic monitoring of both free and total concentrations of palbociclib in plasma.

Results: In this study, we developed a method for the therapeutic drug monitoring of palbociclib in human plasma. The lower limit of quantification for valproic acid was determined to be 1 ng/mL. The calibration curve for palbociclib was validated within the range of 1 to 1000 ng/mL, demonstrating correlation coefficients>0.99.

Conclusions: Additionally, the developed method was employed for therapeutic drug monitoring of palbociclib in real patient plasma samples.

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P051
DETERMINATION OF STRESS CONDITIONS OF NIRMATRELVIR AND RITONAVIR UNDER FORCED DEGRADATION STUDY

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Introduction: Paxlovid is used for treatment in early COVID-19 diagnosis and to prevent more severe symptoms. Paxlovid is a therapeutic combination of two different antiviral drugs, Nirmatrelvir and Ritonavir [1]. This study aimed to determine the stress conditions for photolytic, acidic, alkaline, thermal, and peroxide degradation studies of nirmatrelvir and ritonavir.

Materials and Methods: All working solutions used in the study were dissolved in methanol. 0.1 M HCl was added to the working solutions for acidic degradation and 0.1 M NaOH was added simultaneously in another test tube for alkaline degradation. The solutions were kept at 40 C for different time intervals and different stirring on a shaker. The optimum holding time and shaking speed were determined and analyzed. For thermal degradation was proceed at different temperatures for 6 days. %3 H2O2 was added to the working solutions for oxidative degradation. For photolytic degradations, they were each exposed to UV light at both 254 nm and 366 nm wavelength for 24 hours.

Results: The developed method will be validated according to the ICH guideline in terms of accuracy, intra-day and inter-day precision, linearity etc.

Conclusions: There is no comprehensive degradation study on Nirmatrelvir in the literature yet. Degradation studies on Ritonavir with antivirals such as Lopinavir and Darunavir [2]. The fact that Paxlovid is on the current treatment list and has shown significant and tangible results in the fight against the disease increases the importance of Nirmatrelvir and therefore Ritonavir.

Acknowledgements: This study was supported by a grant of TUSEB (Project No:34518)

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P052

UV-VIS SPECTROSCOPY METHOD ALLIED WITH CHEMOMETRICS FOR SIMULTANEOUS ANALYSIS OF DEXKETOPROFEN TROMETAMOL AND THIOCOLCHICOSIDE IN COMMERCIAL TABLETS

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Introduction: Dexketoprofen trometamol (2-Amino-2-(hydroxymethyl)-1,3-propanediol(S)-3-benzoylalfa methylbenzeneacetate) is an active ingredient with an anti-inflammatory effect. Thiocolchicoside (N-[(7S)-3-(beta-D-glucopyranosyloxy)-1,2-dimethoxy-10-(methylsulfanyl)-9-oxo-5,6,7,9-tetrahydrobenzo[a]heptalen-7 -yl] acetamide) has a muscle relaxant effect. It shows a selective affinity for GABA and glycinergic receptors [1,2]. Herein, simultaneous determination of these active substances was studied using the UV-Vis spectroscopy method allied with chemometrics.

Materials and Methods: Analytical grade methanol is used for preparing the stock solutions (active ingredients and two different commercial tablet drugs'). Binary pharmaceutical combinations containing dexketoprofen trometamol and thiocolchicoside were prepared by applying the central composite experimental design methodology. Measurements of prepared synthetic mixtures were carried out using UV-Vis spectrometry. Chemometric models were created with the Unscambler X10.4 software program. With the help of chemometric methods (principal component analysis (PCA) and partial least squares regression method (PLRS)) data obtained from the UV-Vis spectroscopy.

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Results: Separate calibration graphs were drawn for dexketoprofen trometamol and thiocolchicoside. LOD values of the methods were calculated. For the dual formulation sample analysis containing dexketoprofen trometamol and thiocolchicoside, the LOD was found as 0.0042 mg with R2= 0.99.

Conclusions: The UV-Vis spectroscopy method enables more sensitive and cost-effective measurements compared to other methods. When simultaneously determining mixtures containing two or more active pharmaceutical ingredients, the UV-Vis spectroscopy allied with chemometrics is commonly used. This methodology could be used by combining the analyses with chemometrics, allowing for the simultaneous determination of dexketoprofen trometamol and thiocolchicoside with precise, fast, accurate, and reliable results.

Acknowledgements: This study was supported by a grant of TUBITAK-2209-A (1919B012214257)

P053

INFRARED SPECTROSCOPY COMBINED WITH CHEMOMETRICS FOR SIMULTENOUS RECOGNITION OF DEXKETOPROFEN TROMETAMOL AND THIOCOLCHICOSIDE IN COMMERCIAL TABLETS

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Introduction: Near-infrared (NIR) and mid-infrared (Mid-IR) are two promising techniques which could be utilized for the analyses of drugs and identification of their main constituents. Furthermore, the measurements with an ATR apparatus are performed in a short time with very few samples, without a need for sample preparation protocol. The disadvantage of the method is that it is not easy to interpret the data representing the total composition of the samples from spectral data; thus, the chemometrics evaluations are required to solve this problem (1-3).

Materials and Methods: In this research, studies have been performed on the development of Mid-IR spectroscopy methods allied with PCA and PLSR approaches for the simultaneous determination of dexketoprofen trometamol and thiocolchicoside in binary combinations. The experimental studies were performed in three main stages; (i) preparation of active ingredient combinations by applying CCD methodology, (ii) Mid-IR spectroscopy analysis in the wavenumber ranges of 4000-650 cm-1 for these combinations and (iii) construction of prediction models using chemometrics.

Results: The concentrations of active ingredients in two different commercial tablets were successfully determined by using Mid-IR spectroscopy methods with chemometrics. For the analysis of active ingredient combinations including thiocolchicoside and dexketoprofen, the value of LOD was found as 0.0578 mg with R2=0.9474.

Conclusions: It was concluded that successful findings were obtained by a rapid, inexpensive and nondestructive Mid-IR method allied with the PCA and PLSR prediction models for the simultaneous determination of active ingredients in commercial tablets.

Acknowledgements: This study was supported by TUBITAK (SBAG-115S564) This work was financially supported by a grant of Istanbul–University Cerrahpaşa (Project number: TSA-2023-37231).

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P054

SIMPLE SPECTROPHOTOMETRIC DETERMINATION OF LIPID MODIFYING AGENTS IN A BINARY MIXTURE USING MATRIX RESOLUTION METHOD

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Introduction: Cardiovascular diseases are the leading global cause of mortality. Lipid-modifying agents, like the combination of ezetimibe and rosuvastatin, play a crucial role in managing various cardiovascular conditions by effectively lowering cholesterol. This fixed-dose formulation is commonly prescribed due to enhanced efficacy, reduced side effects, and increased patient convenience. (1) Generally, the quantitative analysis of fixed-dose formulation dosage forms is performed by HPLC. However, simultaneous spectrophotometric analysis of mixtures is favorable because it offers simplicity, speed, and cost-effective equipment. Here, we aim to develop a simple spectrophotometric method (2) using matrix operations for the determination of ezetimibe and rosuvastatin in tablets, despite the presence of overlapping spectra.

Materials and Methods: Standard solutions of each drug were prepared in the range of 4-20 µg/mL in methanol. The spectra of each solution were recorded between 210-350 nm. The absorbance values at 232.8 nm, and 244.0 nm, representing the maximum absorbance wavelengths of ezetimibe and rosuvastatin, respectively, were used to calculate the absorptivity coefficients of each drug. As the absorbance values are additive, two equations describing the absorbance of binary mixtures were generated for the selected wavelengths. The equation pair was represented by the matrix notation to calculate the unknown amounts of drugs in binary mixtures in Microsoft Excel. A set of laboratory-made binary mixtures was prepared for the validation of the method. The commercial samples were then analyzed by the proposed method.

Results: The average absorptivity coefficients at 232.8 nm and 244.0 nm were calculated as 0.065 and 0.055 for ezetimibe, and 0.034 and 0.040 for rosuvastatin. The mean recovery results obtained by applying the proposed method to laboratory-made mixtures were reported to be 98.95% for ezetimibe and 100.30% for rosuvastatin. The proposed method was successfully applied to the analysis of fixed-dose tablets.

Conclusions: The proposed method was found to be simple, fast, and accurate for the analysis of ezetimibe and rosuvastatin in tablets. The method did not require any special software for calculations.

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P055
METHOD DEVELOPMENT BY CAPILLARY ELECTROPHORESIS FOR LORNOXICAM DETERMINATION IN PHARMACEUTICAL TABLETS

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Introduction: Lornoxicam is a non-steroidal anti-inflammatory drug with an analgesic effect, belonging to the classical oxicam group (1). It is used to treat mild to moderate pain caused by extra-articular inflammation. This study aims to develop a validated capillary electrophoresis method to determine lornoxicam in pharmaceutical preparations.

Materials and Methods: The separation of Lornoxicam was conducted in a 48.5cm fused-silica capillary by using a 10 mM borate as a running buffer (pH 9.24) containing 10% (v/v) methanol (2,3).1M NaOH and 0.1M NaOH were used as washing solutions. Lornoxicam (standard) and Rutin (internal standard) samples were prepared with a mixture of methanol and water as a solvent. Different voltage values were applied (25,28 and 30 kV) to optimize the retention time. To obtain the maximum absorbance for standard Lornoxicam different values of wavelength (204, 210, and 380 nm) were tested.

Results: In this study, a simple and rapid capillary zone electrophoretic method was developed for the quantitative determination of the Lornoxicam in the pharmaceutical tablets. Rutin was used as an internal standard. The optimum wavelength and voltage of the method were decided on 380 nm wavelength and 25 kV, respectively. The method showed a good linearity over the range of 1,77x10-5 M to 1,06x10-4M.

Conclusions: The proposed method accurately estimates commercial formulations without being affected by excipients and other additives. Therefore, it is suitable for routine determination of lornoxicam in both pure and pharmaceutical forms.

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P057
EVALUATION OF APIXABAN CRUSHED TABLET SUSPENSION WITH NASOGASTRIC TUBE APPLICATION BY IN VITRO ANALYSIS

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Introduction: Apixaban, a direct oral anticoagulant, plays a crucial role in preventing thromboembolic events. In clinical scenarios where patients cannot swallow intact tablets, administration via nasogastric tube (NGT) as a crushed tablet suspension is necessary. This administration process can be done by using either water or food sources. However, the choice of suspension medium and preparation method can influence drug effectiveness. This study aims to evaluate the impact of different mediums and sample preparations on the chemical effectiveness of apixaban crushed tablet suspension for NGT administration.

Materials and Methods: Waters HPLC system equipped with an UV detector was used for analysis. Analyses have been conducted with the the ACE C18 150 x 4.6 mm, 5µm, analytical column. The mobile phase consisted of acetonitrile: sodium dihydrogen phosphate buffer solution. Detection wavelength was selected as 280 nm. Samples for both reference Eliquis 5 mg Filmtabletten and Paxiban 5 mg Film Coated Tablet are prepared with water, water with %5 dextrose solution, apple juice and apple puree. After sample preparation, all four samples administered through silicon and PVC nasogastric tubes individually and dissolution profiles is examined with 0.1N HCl medium, pH:4.5 acetate medium, pH: 6.8 sodium phosphate medium and pH: 6.8 sodium phosphate medium with 0.05% sodium lauryl sulfate.

Results: Effects of different type of sample preparation methods and different type of nasogastric tube materials examined on this study through comparison between Eliquis 5 mg Filmtabletten and Paxiban 5 mg Film Coated Tablet with 4 different mediums. Eliquis 5 mg Filmtabletten and Paxiban 5 mg Film Coated Tablet dissolution profiles were found similar regardless of the sample preparation method and the material of the nasogastric tube. Dissolution results given below.

Paxiban 5 Mg Film Coated Tablet Dissolution Profiles with Silicon Nasogastric Tube Usage Dissolution Results %								
Time (min)	0.1 N HCl medium				4.5 Acetate with 0.05% SLS medium			
	Sample preparation with water	Sample preparation with apple juice	Sample preparation with %5 dextrose soln.	Sample preparation with apple puree	Sample preparation with water	Sample preparation with apple juice	Sample preparation with %5 dextrose soln.	Sample preparation with apple puree
5	85.1	82.6	80.5	79.2	82.0	82.3	84.2	84.3
10	89.1	86.2	89.1	83.1	92.1	94.1	97.3	91.7
15	89.0	87.6	90.2	86.6	93.2	94.2	97.5	94.4
20	89.5	86.9	91.3	87.5	97.9	94.5	97.2	96.3
30	90.4	87.8	92.5	87.8	99.3	94.0	96.9	95.3

Paxiban 5 Mg Film Coated Tablet Dissolution Profiles with Silicon Nasogastric Tube Usage Dissolution Results %								
Time (min)	pH 6.8 phosphate medium				pH 6.8 phosphate with 0.05% SLS medium			
	Sample preparation with water	Sample preparation with apple juice	Sample preparation with %5 dextrose soln.	Sample preparation with apple puree	Sample preparation with water	Sample preparation with apple juice	Sample preparation with %5 dextrose soln.	Sample preparation with apple puree
5	84.2	80.1	70.4	79.9	97.9	74.1	83.6	73.2
10	91.8	85.2	84.2	91.7	100.1	85.8	92.6	85.9
15	93.5	89.8	90.5	93.3	100.7	89.5	92.0	90.1
20	94.3	90.3	93.4	94.6	100.2	90.9	94.2	90.7
30	95.9	90.7	92.8	94.3	100.5	90.8	94.4	90.9

Paxiban 5 Mg Film Coated Tablet Dissolution Profiles with PVC Nasogastric Tube Usage Dissolution Results %								
Time (min)	0.1 N HCl medium				4.5 Acetate with 0.05% SLS medium			
	Sample preparation with water	Sample preparation with apple juice	Sample preparation with %5 dextrose soln.	Sample preparation with apple puree	Sample preparation with water	Sample preparation with apple juice	Sample preparation with %5 dextrose soln.	Sample preparation with apple puree
5	82.6	81.9	81.7	78.7	83.1	83.1	80.2	85.7
10	87.2	86.9	87.2	82.1	89.9	89.9	92.3	91.5
15	89.3	87.3	89.7	87.5	92.1	92.1	94.3	95.6
20	90.4	87.9	90.1	87.3	93.2	93.2	95.6	96.6
30	90.8	87.1	91.1	88.7	93.8	93.8	95.1	96.1

Paxiban 5 Mg Film Coated Tablet Dissolution Profiles with PVC Nasogastric Tube Usage Dissolution Results %								
Time (min)	pH 6.8 phosphate medium				pH 6.8 phosphate with 0.05% SLS medium			
	Sample preparation with water	Sample preparation with apple juice	Sample preparation with %5 dextrose soln.	Sample preparation with apple puree	Sample preparation with water	Sample preparation with apple juice	Sample preparation with %5 dextrose soln.	Sample preparation with apple puree
5	88.0	79.9	68.1	81.4	98.3	75.5	79.0	73.4
10	93.1	89.8	81.3	90.9	99.1	88.1	89.8	85.9
15	94.3	90.1	88.0	92.3	99.8	90.6	92.4	91.2
20	93.0	92.8	90.2	95.2	99.6	92.2	94.0	90.9
30	95.8	91.6	94.7	94.9	100.8	92.3	94.2	91.2

Eliquis 5 mg Filmtabletten Dissolution Profiles with Silicon Nasogastric Tube Usage Dissolution Results %								
Time (min)	0.1 N HCl medium				4.5 Acetate with 0.05% SLS medium			
	Sample preparation with water	Sample preparation with apple juice	Sample preparation with %5 dextrose soln.	Sample preparation with apple puree	Sample preparation with water	Sample preparation with apple juice	Sample preparation with %5 dextrose soln.	Sample preparation with apple puree
5	84.0	83.6	81.7	78.7	86.0	85.5	85.4	83.0
10	90.1	85.9	87.2	82.1	93.6	92.1	97.2	92.1
15	90.0	87.6	89.7	87.5	96.4	93.2	98.3	93.9
20	89.5	87.9	90.1	87.3	98.4	92.9	98.0	95.3
30	90.5	88.6	91.1	88.7	99.2	92.4	98.2	95.8

Eliquis 5 mg Filmtabletten Dissolution Profiles with Silicon Nasogastric Tube Usage Dissolution Results %								
Time (min)	pH 6.8 phosphate medium				pH 6.8 phosphate with 0.05% SLS medium			
	Sample preparation with water	Sample preparation with apple juice	Sample preparation with %5 dextrose soln.	Sample preparation with apple puree	Sample preparation with water	Sample preparation with apple juice	Sample preparation with %5 dextrose soln.	Sample preparation with apple puree
5	85.3	80.5	73.1	80.7	99.6	78.5	82.6	76.3
10	93.9	86.9	81.9	86.4	100.4	88.0	93.8	86.5
15	94.8	90.5	90.7	92.1	100.7	90.0	93.0	91.7
20	95.2	91.2	93.4	92.7	99.9	92.0	95.5	92.7
30	94.7	90.8	95.3	92.2	100.5	92.3	94.9	92.0

Eliquis 5 mg Filmtabletten Dissolution Profiles with PVC Nasogastric Tube Usage Dissolution Results %								
Time (min)	0.1 N HCl medium				4.5 Acetate with 0.05% SLS medium			
	Sample preparation with water	Sample preparation with apple juice	Sample preparation with %5 dextrose soln.	Sample preparation with apple puree	Sample preparation with water	Sample preparation with apple juice	Sample preparation with %5 dextrose soln.	Sample preparation with apple puree
5	84.0	79.9	81.5	79.9	81.2	84.8	82.6	83.3
10	88.1	85.9	88.7	85.3	88.5	92.1	93.9	92.4
15	89.1	86.9	89.6	88.2	91.1	93.0	95.0	95.6
20	89.5	86.1	90.0	88.3	95.9	93.4	94.7	96.6
30	91.4	88.1	92.2	89.8	95.7	94.5	94.9	96.1

Eliquis 5 mg Filmtabletten Dissolution Profiles with PVC Nasogastric Tube Usage Dissolution Results %								
Time (min)	pH 6.8 phosphate medium				pH 6.8 phosphate with 0.05% SLS medium			
	Sample preparation with water	Sample preparation with apple juice	Sample preparation with %5 dextrose soln.	Sample preparation with apple puree	Sample preparation with water	Sample preparation with apple juice	Sample preparation with %5 dextrose soln.	Sample preparation with apple puree
5	82.8	83.3	76.1	84.9	99.8	77.0	82.6	83.3
10	91.7	90.8	85.4	93.3	100.9	86.5	93.9	92.4
15	94.2	94.0	92.1	94.6	100.8	89.5	95.0	95.6
20	93.9	95.0	96.0	96.1	100.5	91.0	94.7	96.6
30	94.8	94.8	96.8	96.0	100.1	91.5	94.9	96.1

Conclusions: Comparison study between Eliquis 5 mg Filmtabletten and Paxiban 5 mg Film Coated Tablet showed that both drug products behaved similarly in case of different nasogastric tube usage or sample preparation method. Different types of nasogastric tube usage(silicon and PVC) and different sample preparation method (water, water with %5 dextrose solution, apple juice, apple puree) gave similar profile with different dissolution mediums for both product.

Acknowledgements: This study was conducted at Nobel Pharmaceuticals.

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P058

GREEN SYNTHESIS OF SILVER AND ZINC NANOPARTICLES USING PROPOLIS EXTRACTS OBTAINED FROM GİRESUN REGION AND THEIR ANTIMICROBIAL, ANTIBIOFILM AND ANTI-QUARUM SENSING ACTIVITIES

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Introduction: Propolis is a complex natural bee product containing phenolic compounds and flavonoids, obtained from plants by Apis mellifera L. (honey bee). Raw propolis contains 60% resin (consisting of flavonoids, phenolic acid and their polyphenolic fractions), 30% wax, 10% essential and aromatic oils, 5% pollen and other components. The green approaches are safe and environmentally friendly methods for nanoparticle synthesis. Within the scope of this study, AgNPs and ZnNPs were synthesized and characterized using a green method from the ethanol extract of propolis in Giresun region. Following these processes, their antimicrobial, antibiofilm and anti-quarum activities were examined.

Materials and Methods: Propolis extract was prepared in 70% ethanol and filtered. For the synthesis of nanoparticles, the process was started by adding the appropriate amount of extract to salt solutions and set to pH 10. It was incubated in the incubator at 60°C. After this, it was centrifuged, filtered and the precipitate were dried. Characterization studies were performed using UV-visible spectroscopy, fourier transform infrared spectroscopy (FTIR), X-ray diffraction (XRD) and Scanning electron microscope (SEM). For the antimicrobial activity, the MIC (Minimum Inhibitory Concentration) values of the nanoparticles were determined using the broth microdilution method. The anti-QS activity test was performed by the disc diffusion method using reporter bacteria *Chromobacterium violaceum* ATCC 12472. The antibiofilm activity against *P. aeruginosa* PAO1 was evaluated using the crystal violet assay.

Results: Color change, which is the first sign that nanoparticles have been synthesized, was observed as a result of the synthesis procedure. Afterwards, characterization study was carried out using UV-Vis and AgNPs and ZnNPs were detected at 420 and 320 nm, respectively. Functional groups on the NP surface were determined by FTIR. No impurity was observed as a result of the XRD study, and as a result of the SEM study, both nanoparticles were below 100 nm. According to the antibacterial activity results, ZnNPs exhibited the best antibacterial activity against S. aureus ATCC 43300 with a MIC of 0,0625 mg/ml and AgNPs exhibited the best antimicrobial activity against S. aureus ATCC 43300 and S. aureus ATCC 25923 with a MIC of 0,250 mg/ml. Moreover, ZnNPs showed activity against C. albicans ATCC 10231 with an MIC of 0,50 mg/ml. The percentage biofilm inhibition value of ZnNPs and AgNPs was found to be 38.94% and 38.67%, respectively. Synthesized nanoparticles were tested did not exhibit any anti-quotient sensing activity.

Conclusions: According to the characterization results, nanoparticles smaller than 100 nm were synthesized and no impurities were observed. The antimicrobial activity results, NPs showed the best activity against gram-positive bacteria.

Acknowledgements: Nuran GOKDERE thanks the financial support from the Technological Research Council of Turkey (TUBITAK) under the BIDEB/2211-A Ph.D.

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P059
APPLICATION OF BOX-BEHNKEN DESIGN (BBD) ON THE HPLC METHOD DEVELOPMENT FOR ANALYSIS OF ASUNAPREVIR IN PHARMACEUTICAL FORMULATIONS

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Introduction: As stated by WHO, nearly 150 million people worldwide are persistent carriers of hepatitis C virus (HCV), and HCV infection can advance into cirrhosis of the liver and some serious complications, which are accepted to be responsible for more than 350,000 deaths each year. However, as a powerful weapon against such cases, antiviral therapy is found to be effective to decrease the speed of progression and increase survival rate of patients (1). HCV reproduction in hepatocytes involves entry of NS3 and NS4A protease enzymes into the cells, which have crucial role in HCV replication. Accordingly, inhibition of these enzymes turned out to be a notable target in chemotherapy, and protease inhibitors are in use as combination therapy to patients since 2013. Asunaprevir (ASNP), which is a tripeptidic acylsulfonamide inhibitor of HCV NS3/4A protease enzyme, was approved for combination therapy with Daclatasvir in Japan in 2014 (2). In this study, a new HPLC method was developed using Box-Behnken Design approach for quantitative analysis of ASNP.

Materials and Methods: Chromatographic analyses were performed in isocratic mode, and spirodiclofen (SPRD) was found as a suitable internal standard. Supelco Ascentis® Express model column with pentafluorophenylpropyl (F5) functional group (100×4.6 mm, ID, 2.7µm) was used as stationary phase and the mobile phase was acetonitrile:water (90:10, v/v). The flow rate was 0.5 mL/min. Analytical method validation was accomplished according to ICH Q2(R1) guideline. The Box-Behnken Design was used to investigate how ASNP responds to variations in flow rate, mobile phase ratio and injection volume on retention time, peak area and resolution.

Results: The calibration curve was within the range of 0.27 µg/mL to 2.7 µg/mL, and the LOD and LOQ were 0.05 and 0.27 µg/mL, respectively. Total analysis time was under 5 minutes. A good chromatographic separation was obtained under optimal conditions,

Conclusion: A new HPLC approach for determination of ASNP was successfully developed and validated. The method is suggested to be applicable for the quantitative analysis of ASNP in tablet formulations.

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P060
ANALYSIS OF ANTIBIOTIC USAGE AT SHOGAT "PROF. DR. D. STAMATOV," VARNA, BULGARIA, FROM 2017 TO 2023

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Introduction: The emergence of multidrug-resistant and pandrug-resistant bacteria is one of the greatest challenges facing modern medicine. These bacteria are associated with the occurrence of infections both in the community and in hospitals (nosocomial infections), medical centers, and palliative care homes. According to a study by O'Neill et al., antimicrobial resistance seriously threatens human health. By the year 2050, deaths due to resistant bacteria are expected to exceed 10 million per year (1). The most common reasons for the emergence of multidrug-resistant bacteria include increased consumption and improper use of antibiotics, the emergence of mutations in bacteria, the use of antibiotics in livestock farming and agriculture, and others.

The aim of our study is to explore and analyze antibiotic use at SHOGAT "Prof. Dr. D. Stamatov" Varna, Bulgaria, from 2017 to 2023 and assess whether the COVID-19 pandemic has influenced antibiotic usage in the medical facility.

Materials and Methods: We analyzed data from four different wards (Intensive care unit, Maternity ward, Gynecology ward and High-risk pregnancy ward) at SHOGAT "Prof. Dr. D. Stamatov" Varna, Bulgaria. The Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) classification system was used to determine antibiotic consumption, which is an international standard for calculating antibiotic consumption in a unified technical unit - defined daily dose (DDD). A comparative method was applied to assess the quantity of antibiotics used.

Results: As a result of the conducted study, no significant differences were found in antibiotic usage before, during, and after the COVID-19 pandemic. The only observation was the inclusion of Azithromycin as a preferred agent in the therapy of admitted patients with confirmed COVID-19.

Conclusions: Adhering to strict protocols for antibiotic administration in the hospital is one of the most secure methods for limiting the development of antibiotic resistance and the occurrence of nosocomial infections.

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P061

AN ASSESSMENT OF CEFIDEROCOL'S SYNERGISTIC EFFECTS WITH, COLISTIN, TIGECYCLINE, LEVOFLOXACIN, CEFTAZIDIME/AVIBACTAM, AND TRIMETHOPRIM/SULFAMETHOXAZOLE AGAINST MULTI-DRUG RESISTANT STENOTROPHOMONAS MALTOPHILIA

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Introduction: Cefiderocol is a novel siderophore antibiotic that has shown strong in vitro action against Stenotrophomonas maltophilia and multi-drug-resistant (MDR) Gram-negative bacteria, including strains of Enterobacterales, P. aeruginosa, and A. baumannii that are resistant to carbapenem (1). The U.S. Food and Drug Administration (FDA) has authorized cefiderocol for the treatment of nosocomial pneumonia, including ventilator-associated pneumonia, and complex urinary tract infections that are caused by susceptible aerobic Gram-negative bacteria (2). There is insufficient data on cefiderocol combination treatment against MDR S.maltophilia isolates. The objective of this study was to evaluate and compare the in vitro activity of cefiderocol alone and in combination with colistin, tigecycline, levofloxacin, ceftazidime/avibactam and trimethoprim-sulfamethoxazole (TMP-SMZ) against a collection of MDR S. maltophilia isolates.

Materials and Methods: The MICs of cefiderocol and the tested antibiotics for 30 S. maltophilia isolates were determined. Four strains with various cefiderocol MICs were then tested in time-kill experiments with cefiderocol alone and in combination with comparators (3).

Results: The agent for which the susceptibility rate was highest were cefiderocol (100%). Cefiderocol also displayed the lowest MIC50 and MIC90 values. In time-kill experiments, synergy was observed when cefiderocol was combined with levofloxacin, colistin, tigecycline, or TMP-SMZ against 2/4 isolates at 1xMIC concentration.

Conclusions: These data suggest that cefiderocol displays potent in vitro activity against MDR S. maltophilia. According to our results, cefiderocol, combined with levofloxacin, colistin, tigecycline and TMP-SMZ has in-vitro synergy and shows promise as an alternate treatment for treating infections caused by MDR S. maltophilia. These results show that new investigations for cefiderocol are needed, with more complex in vitro and in vivo model studies to define its place in therapy for this pathogen.

Acknowledgements: This work was supported by a grant from the Research Fund of the University of Istanbul (Istanbul, Turkey). Project number: 39819

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P062
DEVELOPMENT AND CHARACTERIZATION OF TAMOXIFEN CITRATE LOADED Ɣ-CYCLODEXTRIN METAL ORGANIC FRAMEWORKS

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Introduction: ɣ-Cyclodextrin metal-organic frameworks (ɣ-CD-MOFs) are novel drug delivery systems prepared with gamma-cyclodextrin and alkali metal cations which constitute a class of porous, edible nanomaterials with high surface area (1). Tamoxifen citrate is widely used for preventing recurrence of ER-positive breast cancers (2,3). It is a BCS II drug, a weak base, characterized with rapid dissolution in the gastric environment with possible precipitation expected due to the high pH in the duodenum (4). In this study, it was aimed to increase the solubility of TMX by preparing TMX-ɣ-CD-MOF formulations and fully characterize the TMX-ɣ-CD-MOFs.

Materials and Methods: Two different ɣ-CD-MOF were prepared by modified methanol diffusion method with slight modifications. Tamoxifen was encapsulated in ɣ-CD-MOFs via impregnation method at 60°C. Loading efficiency was measured by UV spectrophotometry at 235 nm. Characterization studies were carried out using DLS, SEM, DSC, XRD, BET techniques. Solubility studies were performed with TMX-ɣ-CD-MOFs comparatively with pure drug and physical mixture (1:1) in pH 1.2, pH 4.5 and pH 6.8 at 37°C and in water at 25°C.

Results: The formulations were prepared by two methods were named TMX-ɣ-CD-MOF-1 and TMX-ɣ-CD-MOF-2 with particle sizes 606,3±38,40 nm and 337,8±31,86 nm, respectively. The solubility of TMX was successfully increased in pH 1.2, pH 4.5, pH 6.8 and water with ɣ-CD-MOF formulations. TMX-ɣ-CD-MOF-2 found to be more successful in enhancing solubility of TMX, considered to be a result of its lower particle size.

Conclusions: ɣ-Cyclodextrin metal-organic frameworks (ɣ-CD-MOFs) are promising novel drug delivery systems to enhance solubility hence dissolution rate of BCS II and IV drugs.

Acknowledgments: This study was supported by a grant of TÜBİTAK (SBAG-222S923).

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P063
DEVELOPMENT AND CHARACTERIZATION OF ACTIVE TARGETED GOLD NANOPARTICLES FOR TUBERCULOSIS TREATMENT

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Introduction: Tuberculosis (TB) is a chronic respiratory disease caused by Mycobacterium tuberculosis (Mtb) (1). Linezolid (Lin), an oxazolidinone antibiotic, effective against Gram-positive bacteria, has shown strong efficacy against drug-resistant Mtb strains in laboratory and animal tests (2). In recent years, the rise of widespread drug-resistant strains has made treating this disease more complex Formun Üstü(3). Nonetheless, employing targeted drug delivery systems loaded with active substances can mitigate the situation (4). In our study, we aimed to develop an effective drug delivery system for TB. Gold nanoparticles (AuNPs) were synthesized as the carrier system and modified with mercaptoundecanoic acid (MUA), mercaptopropionylaminoethyl ortho polyethylene glycol (SH-PEG) and a targeting agent (antibody). The objective of this study was to develop Lin-loaded AuNPs to enhance treatment efficacy with lower doses and reduce side effects through targeted drug delivery.

Materials and Methods: AuNPs were synthesized via the Turkevich method (5). Confirmation of chemical bindings at each stage of formulation preparation was achieved by assessing alterations in band patterns via Attenuated Total Reflection (ATR) measurements, absorbance changes in UV spectroscopy and changes in particle size (PS), polydispersity index (PDI) and zeta potential (ZP) analyzed using the Malvern Zetasizer instrument. Raman spectroscopy confirmed Ab binding. Lin quantitative analyses were performed and validated in UV-VIS spectroscopy at pH 7.4. In vitro release studies were performed using Franz cells and encapsulation efficiency (EE) was determined by the indirect method.

Results: Results from characterization techniques including ATR, UV, and Raman spectroscopy demonstrated modification evidence. Following optimization studies, nanoparticles with a size of 120-140 nm, a PDI value of 0.4 and a zeta potential of -20 mV were obtained. In vitro release studies showed that the release of the active substance was completed in 8 hours.

Conclusions: In this study, a nanoscale active targeted drug delivery system, which is expected to be effective against TB, was successfully prepared and characterized.

Acknowledgments: This study was supported by Gazi University Scientific Research Projects Coordination Unit under grant number TCD-2023-8426. Linezolid was generously gifted by Biofarma Pharmaceuticals (Turkey).

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P064
IN VITRO EVALUATION OF EMULGEL AND NANOEMULGEL FORMULATIONS OF DICLOFENAC POTASSIUM FOR TOPICAL APPLICATION

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Introduction: Diclofenac potassium is a non-steroidal anti-inflammatory drug that is commonly used for controlling pain and inflammation. Diclofenac potassium is a Class II compound according to the Biopharmaceutics Classification System (low solubility and high permeability) (1, 2). The aim of this study was to develop emulgel and nanoemulgel formulations of diclofenac potassium, prepared using Carbomer and penetration enhancing excipients and evalute the formulations in vitro.

Materials: Diclofenac potassium, isopropyl alcohol, propylene glycol, carbomer 980, liquid paraffin, Tween 20, Span 20, PEG 400 and glycerine were obtained from Sigma Aldrich. HPLC-grade acetonitrile and methanol were purchased from Merck (Germany). The water was purified by Direct-Q® 3 UV water purification system (Millipore, USA). All other chemicals used were of analytical grade and were used without any further chemical modification.

Methods: The developed HPLC method was validated in terms of selectivity, linearity, precision, sensitivity, and accuracy and was used for the determination diclofenac potassium. The formulations were evaluated for their physical appearance, pH, rheological properties, viscosity, drug release and stability tests.

Results: The linearity of the method was evaluated within the range of diclofenac potassium concentrations of 2.5-40 µg/mL. The calibration curve equation calculated using linear regression analysis was y=19429.2x-5246.95. A good linear relationship was established between the peak areas and the concentrations (2.5-40 µg /mL) of diclofenac potassium with the determination coefficient (R2)=0.9999.

Table 1. Characterization of the formulations

	Emulgel	Nanoemulgel
Appearance	White viscous creamy	White viscous creamy
pH	6.45± 0.02	6.01± 0.04
Viscosity (cp)	956±25	812±21
Drug Content	96.6±1.5	95.2±1.6
Spreadability (Diameter of circle)	3.15± 0.13	3.77± 0.11
Amount of release of drug after 6 hour	51.6± 7.26%	62.2± 6.31%

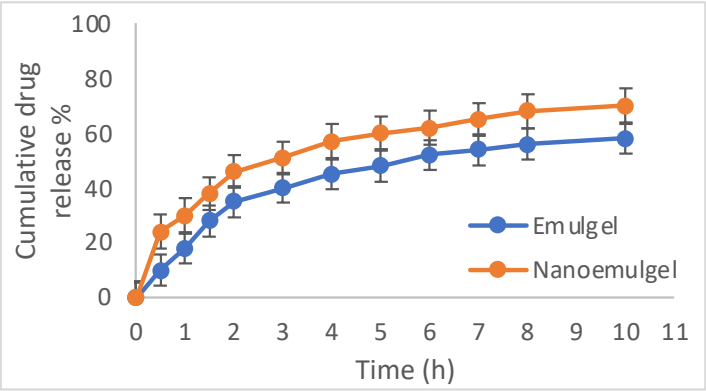

Figure 1. Drug release profile of diclofenac potassium

Conclusions: Topical emulgels of diclofenac potassium were formulated and characterized to physicochemical studies i.e. rheological studies, spreading coefficient studies and in vitro release studies. In vitro release of the formulations were performed to determine drug release rate from emulgel and nanoemulgel formulations.

Acknowledgements: There is no institution supporting the study.

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P065
DETERMINATION OF CRITICAL MICELLE CONCENTRATION OF POLYMER MIXTURES BY DONOR-ACCEPTOR INTERACTION WITH IODINE

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Introduction: Critical micelle concentration (CMC) is the minimum concentration of the amphiphilic polymers required to self-assemble into micelles in solution. Various techniques can be used to determine CMC. Among these, the UV-visible spectroscopy is the most common technique due to the availability of instrument and the short analysis time (1). The aim of this study was to investigate the CMC of amphiphilic polymer (Soluplus®, Pluronic® F127 and Pluronic® F68) mixtures by a spectroscopic method.

Materials and Methods: Soluplus®, Pluronic® F127 and Pluronic® F68 were kindly gifted by BASF (Germany). Binary polymer mixtures (1:4, 2:3, 3:2, 4:1) containing Soluplus® and Pluronic® F127, Soluplus® and Pluronic® F68, and Pluronic® F127 and F68 were prepared. CMC values were determined by the formation of electron donor-acceptor complexes with iodine (2). Briefly, a series of polymer solutions was prepared in the range of 0.00001-20 mg/mL in distilled water. The iodine standard solution (ISS) was prepared by dissolving potassium iodide (2%) and iodine (1%) in distilled water. A fixed amount of ISS (25 µL) was added to each polymer solution. After 12 h of incubation at 25 °C, the absorbance was measured at 366 nm using a UV-visible spectrophotometer (Agilent Tech. Cary 60 UV-Vis, USA). The absorbance values were plotted against the logarithmic polymer concentration (log C). The CMC value was calculated by corresponding polymer concentration where a sharp increase in absorbance was observed. The experiments were performed in triplicate.

Results: The CMC values of Soluplus®, Pluronic® F127, and Pluronic® F68 were 7.65; 1578 and 4516 mg/L, respectively, complying with the literature (3, 4). The CMC values of Soluplus®:Pluronic® F127, Soluplus®:Pluronic® F68, and Pluronic® F127:Pluronic® F68 binary mixtures (1:4, 2:3, 3:2, 4:1) were in the range of 1323-1998, 1272-3008 and 2743-3358 mg/L, respectively. Soluplus® decreased the CMC values of Soluplus®:Poloxamer® mixtures, especially the Pluronic F68® ones.

Conclusions: The present study revealed that this spectroscopic method is suitable for the rapid and simple determination of CMC values of Soluplus®, Pluronic F127®, and Pluronic F68® mixtures as a reliable measure of the thermodynamic stability in the development of micellar drug delivery systems.

Acknowledgements: This study was supported by Gazi University, Projects of Scientific Investigations under the project number: TDK-2023-8489.

References:

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P066

PREPARATION AND IN VITRO EVALUATION OF OPHTALMIC MICROEMULSION FORMULATIONS OF MOXIFLOXACIN HYDROCHLORIDE

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Introduction: Moxifloxacin hydrochloride is a fourth generation synthetic fluoroquinolone antibacterial agent. It is often preferred in eye preparations to treat eye infections, including bacterial conjunctivitis. The aim of this study was to develop microemulsion formulations containing moxifloxacin hydrochloride for ophthalmic use and to evaluate their in vitro characterization (1).

Materials: Moxifloxacin hydrochloride was a present material from İlko Ilac¸ San. Tic. A.S¸ (Ankara, Turkey). Isopropyl palmitate, mannitol, benzalkonium chloride solution, Tween 20, propylene glycol and dimethicone were bought from Sigma-Aldrich, Germany.

Methods: High pressure liquid chromatography (HPLC) method was developed and validated for use in quantification and characterization studies (20-200 µg/mL). Solubility studies were conducted to determine the solubility of the active substance in different oils, surfactants and co-surfactants. Pseudo-ternary phase diagrams were obtained with a water titration method at room temperature (25°C). The pseudo-ternary phase diagram of the largest area was selected to determine the concentration range. The mean droplet size and size distribution (polydispersity index; PDI) of microemulsions were characterized and in vitro release tests were performed using dialysis membrane methods.

Results: In vitro drug release profile is presented in Figure 1 and pseudo-ternary phase diagrams are presented in Figure 2. The microemulsion formulations 3:1 ratio was selected from the systems which showed larger microemulsion regions. In this study, a microemulsion sized around 269.8 nm was formed.

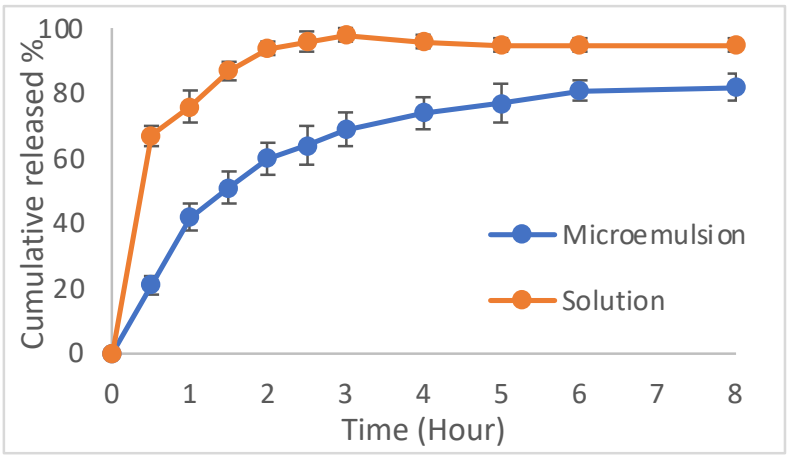

Figure 1. In vitro cumulative drug release profile

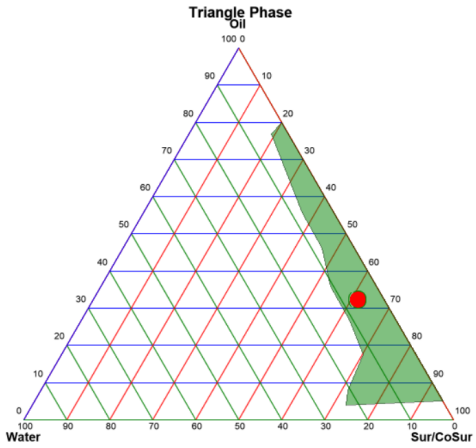

Figure 2. Pseudo-ternary phase diagrams of microemulsions *surfactants:cosurfactant ratio (3:1)

Conclusions: This study shows that the o/w microemulsion with good clarity, ideal stability and suitable characterization, can be prepared successfully using Tween® 20 as the surfactant and propylene glycol as the cosurfactant. Tween® 20: propylene glycol in the weight ratio of 3:1 was the surfactant providing greater area. The in vitro studies demonstrated the potential of developed microemulsion for ophtalmic delivery of moxifloxacin hydrochloride.

Acknowledgements: There is no institution supporting the study.

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P067
ENHANCING THE AQUEOUS SOLUBILITY OF LORNOXICAM VIA CYCLODEXTRIN COMPLEXATION

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Introduction: Lornoxicam (LRX) is a low soluble non-steroidal anti-inflammatory drug (NSAID) (1). The aim of this study was to evaluate the effects of three different cyclodextrins (CDs) on the water solubility of LRX.

Materials and Methods: LRX was kindly provided by Abdi İbrahim Pharmaceuticals (Türkiye). Aiming to improve the water solubility LRX three types of CD derivative β-CD, HP-β-CD and SB-β-CD were investigated in various ratios1:0.5, 1:1, 1:2, 1:4, 1:6 and 1:8 (drug/CDs), by preparing CD complexes using the kneading method (2). For this purpose, LRX and CDs were weighed and triturated with a small volume of water/ethanol (1:1). The slurry obtained was kneaded for 30 min and then left to dry at 37°C for 24 h. Equilibrium solubility studies were carried out by adding excess amount of pure LRX or LRX:CD complexes to vials containing 5 ml water. The vials were stirred at 37±0.5°C for 24 h, then the samples were filtered, absorbance of samples were measured at 376 nm by a UV/Vis spectrophotometer.

Results: While the solubility of pure LRX in water was 27.3 ± 3.3 µg/ml, it was observed that the solubility was increased with the complexation process with CDs. Among the CD derivatives investigated, the highest solubility was observed with SB-β-CD at a molar ratio of 1:8 and the solubility of LRX in water was found to be 74.5 ± 0.3 µg/ml.

Conclusions: To conclude, solubility of LRX in water was affected by the type and ratio of cyclodextrin. It was observed that the solubility enhanced with increasing molar ratios of CDs. Various complexing techniques or different CD types could be furtherly investigated to choose optimum CD type and ratio for maximum solubility enhancement.

Acknowledgements: This study was supported by Gazi University Scientific Research Projects Coordination Unit (BAP) (Project Number: TDK-2022-7536). Yilmaz A. was supported by scholarships from the CoHE 100/2000 PhD Scholarship Program and by TUBITAK 2211/A Domestic PhD Scholarship Program.

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P068

INVESTIGATING THE IMPACT OF DISSOLUTION METHOD ON THE DISSOLUTION PROFILE OF LORNOXICAM-LOADED TABLETS FABRICATED VIA FDM-3DP TECHNOLOGY

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Introduction: Lornoxicam (LRX) is a low-soluble non-steroidal anti-inflammatory drug (NSAID) that exhibits pH-dependent solubility (I). The aim of this study is to develop LRX loaded tablets using HME-based FDM 3DP technology and to investigate their dissolution profiles using Apparatus I and Apparatus II.

Materials and Methods: LRX (LRX) was kindly provided by Abdi İbrahim Pharmaceuticals (Türkiye). Tablets obtained from two different filament formulations were designed with 15*15*2.4 mm3 size, 100% infill density and printed at 170 °C. Formulation contents of tablets are displayed in Table.

Table 1. Formulation contents of F1 and F2 tablets

Formulation codes	LRX (%)	Soluplus® (%)	METHOCEL™ E5 Premium LV (%)	Sodium bicarbonate (%)	Kollidon® 12 PF (%)	Triacetin: Kollisolv® PEG 400 (%)
F1	2.5	70	10	-	10	7.5
F2	2.5	60	10	10	10	7.5

Dissolution studies were performed with USP Apparatus I and USP Apparatus II in 900 ml of 0.1 N HCl with 2% SLS, at 37 ± 0.5 °C with a speed of 50 rpm under sink condition (n=3). 5 ml of samples were withdrawn at specific intervals (5, 10, 15, 20, 30, 45, 60, 90, and 120 minutes) and replenished with an equal volume of fresh media after each withdrawal. The withdrawn samples were analyzed using a UV/Vis spectrophotometer at 376 nm for LRX content.

Results: Due to the pH-dependent solubility of LRX, sodium bicarbonate which, added to the F2 formulation as an alkalizing agent, increased the dissolution of LRX in both methods. The dissolution rate of F2 formulation was found to be higher with Apparatus I compared to Apparatus II.

Conclusions: The reason of the LRX dissolution difference between the methods, especially for the F2 formulation, can be attributed to the floating of the tablets in the vessel.

Acknowledgements: This study was supported by Gazi University Scientific Research Projects Coordination Unit (BAP). Yilmaz A. was supported by scholarships from the CoHE 100/2000 PhD Scholarship Program and by TUBITAK 2211/A Domestic PhD Scholarship Program.

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1. Tawfeek, H.M., et al. Transfersomal gel nanocarriers for enhancement the permeation of lornoxicam. Journal of Drug Delivery Science and Technology, 2020. 56: p. 101540.

P069
THE EFFECT OF FREEZE-DRYING ON THE CHARACTERISTICS OF RIBOFLAVIN-LOADED NANOPARTICLES FOR THE PHOTODYNAMIC THERAPY

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Introduction: Photodynamic therapy is a clinically approved treatment method that can have a selective effect against malignant tumors. It consists of the application of photosensitizing substances followed by irradiation at a certain wavelength (1). Riboflavin (Rf), known as vitamin B2, leads to the formation of reactive oxygen species such as singlet oxygen and hydrogen peroxide under UV-blue irradation. (2,3). In this study, Rf-loaded PLGA nanoparticles (NPs) were developed and characterization studies were carried out before and after freeze-drying process.

Materials and Methods: Nine different NPs formulations were prepared by nanoprecipitation method. Briefly, 2% of PLGA and 0,1% of Rf were dissolved in DMSO and this solution was added dropwise under stirring to 10 mL of water phase containing different ratios of Pluronic F127 (PF127), polyvinyl alcohol or Tween 80. After 1 hour of mixing, particle size, PDI and zeta potential values were measured. The prepared nanoparticles were freeze-dried by adding with/without 1% mannitol solution.

Results: The particle sizes of NPs prepared with PF127 and Tween 80 were below 150 nm and they have highly negative zeta potentials. Generally, it was observed that freeze-drying process increased PDI values and particle sizes for all formulations except RF5 coded formulation which prepared without mannitol.

Conclusions: Among the prepared formulations, RF5 coded nanoparticle formulation (without mannitol) was considered as most promising formulation according to particle size (131,80±0,72 nm), PDI values (0,398±0,026) and zeta potential (-27,93± 0,61 mV) for photodynamic therapy.

Acknowledgements: Maide Öztürk is supported by TUBITAK 2211-C grant.

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P070
STUDIES ON THE FORMULATION OF TWO DIFFERENT MODEL BIOLOGICALLY ACTIVE SUBSTANCES

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Introduction: Biotechnological products have recently become an important group of drugs used especially in cancer diagnosis and treatment. OVA and BSA are model proteins that are often used alone in many studies for biotechnological drug development (1). The main purpose of this study is to prepare nanoparticle formulations containing combined model proteins, to evaluate model protein-loaded nanoparticles systems in terms of various parameters and to show that they can be obtained.

Materials and Methods: Nanoparticles were prepared by the emulsion formation– solvent evaporation method. Mixing speed, polymer/model protein ratio and model protein/model protein ratio parameters were selected among the parameters affecting the physical and chemical properties of the formulations. On these selected parameters, box behnken factorial design, five center points and 17 analysis formulations were obtained (2). The 17 formulations obtained were evaluated in terms of particle size, polydispersity index and zeta potential,

Results: In line with the determined parameters, the formulation criteria for the area with the smallest particle size within the area we scanned, zeta potential greater than -20 and pdI value between 0.1-0.25 were determined. We showed that the final re-prepared formulation showed the determined parameters, and that we successfully loaded two model proteins through release, loading efficiency and stability studies. As a result of the evaluation, it was observed that the model protein ratios were one to one, the polymer to model protein ratio was the lowest and the mixing speed was the highest, it had the smallest particle size and homogeneous distribution.

Conclusions: It has been shown that the model two protein-loaded nanoparticle formulation exhibits the desired in-vitro chemical properties and that the particulate structure is formed. As a result of the release and SDS-PAGE analysis study, it was shown that the model proteins were released into the medium successfully. Thus, it created a basis for more comprehensive studies and in-vivo evaluations.

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P071

DESIGN OF EXPERIMENT APPROACH TO MODELING THE EFFECTS OF FORMULATION ON DRUG RELEASE FROM LIPID NANOCAPSULES

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Introduction: Lipid nanocapsules (LNCs) are nanoparticular systems consisting of an oily liquid core surrounded by a hydrophilic and lipophilic rigid surfactant shell (1). In this study, niclosamide (NIC), a highly hydrophobic molecule, was used as a model drug. The main aim of the current research is to optimize and investigate the influence of various input variables, namely drug concentration percentage (X1), lipid percentage ratio (X2) and hydrophilic surfactant percentage ratio (X3) on drug release (DR) of the NIC loaded LNCs (NIC-LNCs).

Materials and Methods: Box Behnken experimental design was used for the optimization of LNC formulations (Table 1). The design was implemented to investigate the effects of X1, X2 and X3 on the response, DR at 30 days. The levels of variables used in the preparation of NIC-LNCs were shown in Table 1. NIC-LNCs were prepared according to the phase inversion technique (1). In vitro drug release profile of NIC from the LNCs was determined by dialysis method. The bag was immersed a phosphate buffer saline (pH 5.5) with 0.5% tween 20 and 5% methanol at 100 rpm and 37°C. The amount of drug released was determined by HPLC.

Results: Drug releases at the end of 30 days of the LNCs ranged from about 13 to 36%. According to the ANOVA results, X1, X2 and X3 variables had a statistically significant effect DR response ($p < 0.0001$) (Fig 1). As the X1 was increased, DR was decreased. As the X2 increased, DR decreased due to enlargement of the LNC core and the extending of the diffusion distance. As the X3 increased, the particle size decreased and DR increased. Pure drug suspension demonstrated low drug release pattern compared with NIC-LNCs (Fig 2a).

Conclusions: The NIC-LNC formulations exhibited sustained release properties. The highest release rate was obtained at high X2 and low X3 in LNC12 formulation with small particle size (Fig. 2b). LNC improved the dissolution rate of NIC. LNC systems could be good drug carrier for hydrophobic drugs.

Acknowledgements: This study was supported by TUBITAK with 123S083 project number.

Table 1. Factorial design points and the response variable

Code	Variable Levels			Response Variable	
	X1	X2	X3	Actual Value	Predicted Value
LNC1	-1	-1	0	33.64	32.57
LNC2	+1	-1	0	17.69	18.30
LNC3	-1	+1	0	18.55	18.23
LNC4	+1	+1	0	12.93	13.91
LNC5	0	0	0	21.92	22.30
LNC6	-1	0	-1	21.96	22.43
LNC7	+1	0	+1	19.38	20.12
LNC8	-1	0	+1	28.34	31.34
LNC9	+1	0	-1	15.39	14.10
LNC10	0	-1	-1	24.18	24.64
LNC11	0	+1	-1	14.95	14.66
LNC12	0	-1	+1	36.00	34.15
LNC13	0	+1	+1	23.27	21.05

Coded Values	Actual Values		
	X1	X2	X3
-1	2 %	10 %	10 %
0	4 %	20 %	20 %
+1	8 %	30 %	40 %

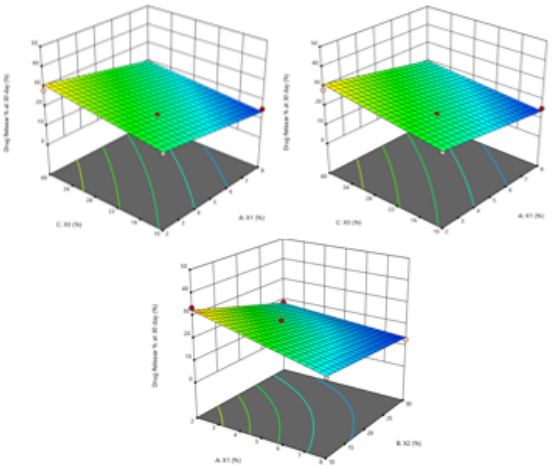

Fig.1. RSM graphs for the effects of independent variables on DR

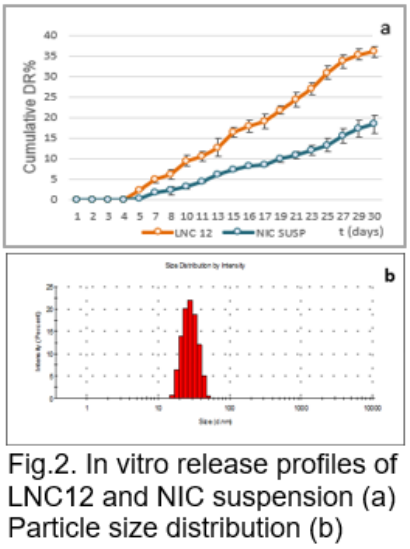

Fig.2. In vitro release profiles of LNC12 and NIC suspension (a) Particle size distribution (b)

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P072
PREPARATION OF KHELLIN-CONTAINING NANOFIBERS VIA ELECTROSPINNING FOR THE TREATMENT OF VITILIGO

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Introduction: Vitiligo is an autoimmune disease of unknown etiology characterized by loss of pigmentation due to melanocyte destruction in the skin, with a prevalence of 0.5-2% worldwide (1). Khellin, an important component of the Ammi visnaga plant used in the traditional treatment of vitiligo, has a unique effect on the first choice of psoralen ultraviolet A (PUVA) treatment. The use of khellin in the treatment of vitiligo has less phototoxic, photochemical and carcinogenic effects and UVA is not required for khellin activation. In this study, khellin-containing nanofiber formulations were fabricated, which may eliminate the need for UVA and improve patient compliance.

Materials and Methods: Khellin was purchased from Santa Cruz (Ammi visnaga plant, SC-206054). Different polymer solutions (10%, 12.5%, 15%, 17.5%, 20% w/v of PVP and 3% w/v of khellin) were prepared in ethanol and nanofibers were produced via electrospinning method. Viscosity, conductivity and surface tension values of polymer solutions were measured (2). The morphology and mean diameter of nanofibers were evaluated with SEM images. In addition, mechanical (tensile strength and elongation at break) and wettability properties of nanofibers were analyzed.

Results: The addition of khellin increased the conductivity compared to the polymer solutions without khellin. In contrast, adding khellin did not affect surface tension and conductivity values. The viscosity values were directly affected by PVP concentration and measured between 391-1448 cps. The tensile strength and elongation at break values of the khellin-containing nanofibers resulted in lower values. The SEM images showed that the increased PVP concentration provided homogeneous fiber morphology and increased nanofiber diameter. The average diameters of the nanofibers were measured between 576-2282 nm. All formulations wetted instantly due to the hydrophilic nature of PVP.

Conclusions: This study is the first khellin-containing nanofiber study in the literature. The results showed that khellin-containing nanofibers could have the potential as a drug delivery system for vitiligo treatment that patients can easily use. Further studies are needed to demonstrate the efficacy of the formulation.

Acknowledgments: This study was supported by a grant from The Scientific and Technological Research Council of Turkey (TUBITAK 2209-A Research Project Support Programme for Undergraduate Students, 1919B012301274).

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P073
FORMULATION STUDIES OF LETROZOLE INCORPORATED KOLLIDON® SR POLYMERIC PARTICLES

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Introduction: Letrozole (LTZ) is a selective non-steroidal aromatase inhibitor with effective anticancer properties (1). Its low solubility in water and having lots of side effects limit its pharmaceutical use. For this reason, the aim of our study was, formulation of novel drug delivery systems in order to increase the therapeutic effect of LTZ while minimizing the side effects with efficient anticancer activity.

Materials and Methods: LTZ was purchased from Sigma (Germany) and Kollidon® SR (KSR) was gifted kindly by BASF (İstanbul, Turkey). All other chemicals were in analytical grade. Nanoparticles were prepared by spray drying method (2). In vitro characteristic properties of the nanoparticles were evaluated in detail. LTZ amount was evaluated by a modified HPLC method. Morphological analyses like particle size (PS), particle size distribution (PdI), zeta potential (ZP) values and in vitro release studies had been conducted within the scope of the characterization studies of the prepared nanoparticles. Anticancer activity of the formulations were evaluated by MTT cytotoxicity method on BJ healthy cell line and Hep G2 liver cancer cell lines.

Results: Formulations were prepared by different amounts of LTZ in order to achieve highest incorporation efficiency (Table 1). MK3 formulation was selected as an ideal formulation and therefore SEM, FTIR, 1H-NMR and in vitro release analysis results were presented in Figure 1-Figure 4 respectively. No cytotoxic effect was observed on the BJ cell line. On the Hep G2 cell line; while the cytotoxic effect was found to be >250 micromolar/ml in MK-3 and, this value was found to be >125 micromolar/ml in LTZ.

Table 1. Compositions of the formulations prepared (Mean±SE; n=3).

CODE	KSR (g)	LTZ (%)	Methanol (mL)	Size (nm)	PdI	ZP (mV)
MKPL	2	-	250	270.0±20.6	0.43±0.03	-16.7±1.3
MK1	2	10	250	287.0±14.3	0.47±0.05	-17.3±0.8
MK2	2	15	250	322.0±17.0	0.52±0.02	-18.3±0.4
MK3	2	20	250	380.0±23.3	0.50±0.05	-21.5±0.6

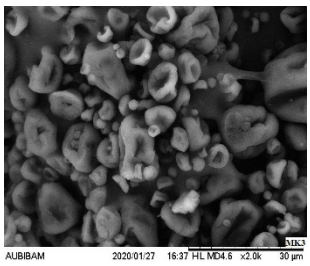

Figure 1: SEM microimage

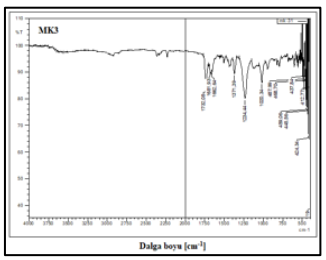

Figure 2: FTIR spectrum

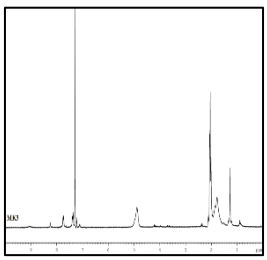

Figure 3: [1]H-NMR spectrum

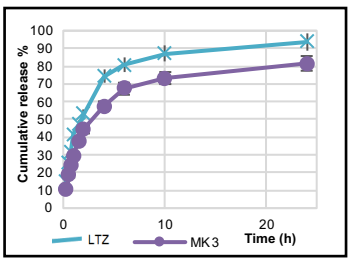

Figure 4: In vi- tro release

Conclusions: The in vitro analyses results revealed that LTZ incorporated polymeric nanoparticles were prepared successfully by spray drying method. Extended releases up to 24 hours were achieved with the help of polymeric nanoparticles which will enhance the potential use of the formulation in cancer treatment while protecting the healthy cells.

Acknowledgement: MER-LAB (FT-IR and [1]H-NMR), BIBAM (SEM)

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P074
PREPARATION AND CHARACTERIZATION OF FAST DISSOLVING TRIAMCINOLONE ACETONIDE ORAL FILM FOR RECURRENT APHTHOUS STOMATITIS

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Introduction: Particular requirements of the patients not compliance to other conventional oral solid delivery systems led to the introduction of new oral dosage forms that have been expected to enhance therapeutic effects and improve patient compliance or develop currently available ones. (1). Triamcinolone Acetonide (TA) is one of the long-acting synthetic glucocorticoids that has been studied for being effective in relieving the anti-inflammatory, antiallergic and immunosuppressive effects (2). The aim of this study was to develop TA orodispersible film (ODF) with fast disintegration time, improved patient compliance and suitable mechanical strength to treat recurrent aphthous stomatitis symptoms in patients not compliance to other conventional oral solid delivery systems to increase compliance and convenience.

Materials and Methods: TA (gifted by DEVA Holding, Turkey). All other chemicals were in analytical grade. Solvent casting method has been used including different polymers and plasticizers with different ratios. A modified UV-Vis spectroscopy method was used for the determination of TA (3). The resultant films were evaluated for disintegration time, folding endurance, surface pH, weight variation, thickness, surface morphology, drug content, content uniformity, moisture loss, moisture uptake, drug-excipient compatibility using differential scanning calorimetry and fourier transform infrared spectroscopy, and dissolution (3). While the content uniformity of Film B was 99.4961± 0.2470, meaningless results were obtained for Film A.

Results: Compsition of the formulations and characterization studies of the resultant films are summerized in Table 1. Resultent transparent film (Fig 1.), Drug release profile (Fig. 2)

Table 1. Compositions and characterizationsof ODF (Mean ± SE, n=3)

Film Code	TA (mg)	HPMC (mg)	PEG 400 (µL)	Tween 80 (µL)	Citric acid (mg)	Sucrose (mg)	Water+ ethanol (mL)	Thickness (µm)	pH	Folding Endurance	Disintigration time (sec.)
A	88	1250	500	50	2	2	50	10,03±0,1488	4,60±0,0001	296,25±6,5511	10,75±0,8660
B	88	1500	200	-	2	2	45	15,87±0,1633	4.75±0,0158	179,25±7,5	22.25±0,9574

Figure 1. Non-sticky transparent film separated from petri dish.

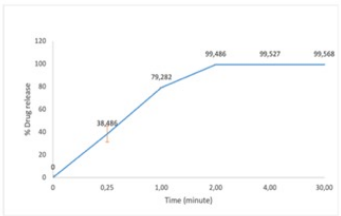

Figure 2. % Drug release profile of B films.

Conclusions: Approximately 5 mg of TA was obtained in most of our formulations with a pH within the range of normal pH of the oral cavity and this indicates the suitability of this dosage form and successful of solvent casting method in preparing 5 mg TA films.

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P075
DEVELOPMENT AND CHARACTERIZATION OF POSACONAZOLE LOADED SELF NANOEMULSIFYING FORMULATION

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Introduction: Self nanoemulsifying drug delivery systems (SNEDDSs) are isotropic mixtures of oils, surfactants, and cosurfactants that constitute nanoemulsions upon agitation of the gastrointestinal system. These systems can be used to increase the oral bioavailability of highly lipophilic drug components (1). Posaconazole is a highly lipophilic antifungal agent which exhibits low and variable bioavailability (2). The aim of this study was to develop posaconazole loaded SNEDDS for oral delivery.

Materials and Methods: The solubility of posaconazole in different oils, surfactants, and cosurfactants was determined. Pseudo ternary phase diagrams were constructed by titration based on preliminary studies, the surfactant/co-surfactant ratio was set at 1:2 (3). Capryol 90® or Capmul MCM® was chosen as the oil phase, Tween 80® as the surfactant and Transcutol HP® as the co-surfactant, based on solubility studies, pseudoternary phase diagrams and morphological parameters. In addition, Soluplus® was added to formulation which is known as precipitation inhibitor (4). SNEDDSs were evaluated in terms of emulsification time, droplet size, polydispersity index, zeta potential and viscosity.

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Results: 15 mg of posaconazole was loaded to 1 g of the formulation successfully. The formulation has bluish-white appearance and its emulsification time was less than one minute which is considered as Grade B. The mean droplet size of the formulation was found 243.37 nm± 66.74 with a a polydispersity index of 0.38± 0.14, and the zeta potential was found -8.27± 0.85 mV whereas the viscosity of the formulation was measured 310.62± 4.37 cP.

Conclusions: The formulation which consists of 15 mg posaconazole, 15% Capryol 90®, 8% Tween 80, 57% Transcutol HP®, and 20% Soluplus® was developed and characterized successfully. Further studies will be conducted to evaluate the formulation's stability, in vitro release, cytotoxicity, and intestinal permeability.

Acknowledgements: This study was supported by a grant of Erciyes University Scientific Research Projects Coordination Unit (FDK-2021-10902). The authors would like to thank Abdi İbrahim for providing posaconazole.

P076
DEVELOPMENT OF MAGNETIC METAL ORGANIC FRAMEWORKS AS DRUG DELIVERY SYSTEMS

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Introduction: Metal-organic frameworks (MOFs) are porous composites composed of metal ions and organic ligands. Due to their large surface area, high drug loading/encapsulation efficiency, and biocompatibility/biodegradability, they are used as drug delivery systems (DDS) in various diseases, especially cancer (1,2). This study aims to overcome problems in conventional chemotherapy such as high drug doses and dose-related side effects by designing an DDS. Tamoxifen (TAM) was chosen as the anticancer drug.

Materials and Methods: Quantification of tamoxifen and validation of the method were performed with a UV spectrophotometer at a wavelength of 235 nm. Magnetic MOF (mMOF) was generated from Fe3O4 nanospheres by the solvothermal method (see Figure 1).

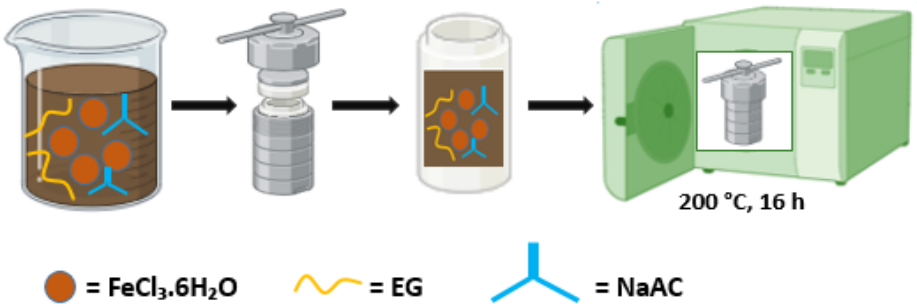

Figure 1. The synthesis procedure of Fe_3O_4 nanospheres

For MOF growth, its modification with mercaptoacetic acid (MAA) was performed. Synthesizing porous mMOF [Fe_3O_4@MIL-100 (Fe)] was carried out in two steps using the step-by-step assembly method. In the first stage, Fe_3O_4 was combined with $FeCl_3.6H_2O$ with MAA. In the second step, magnetic nanoparticles were mixed with trimesic acid (H_3btc). This cycle was repeated 31 times to obtain mMOF. Since the targeting capacity alone was low, the antibody was bound and pegylation (SH-PEG-NH_2) was performed. Tamoxifen was loaded with DDS (Ab-PEG-MOF) by mixing for 24 h. Various characterizations [TEM, Particle Size (PS) and Zeta Potential (ZP)-Malvern Zetasizer Nano, England] were performed to determine the most suitable formulation. The encapsulation efficiency of Magnetic MOF was evaluated.

Results: The analytical method used for TAM was validated and found to be safe to use. Encapsulation efficiency (EE) was examined with certain amounts of mixtures of MOF and TAM. The best EE was seen in Ab-PEG-MOF-TAM prepared with MOF and TAM in a 1:1 ratio (EE: 95.1%). Free MOF; PS: 564.3 nm ZP: -17.2 mV and MOF-PEG; PS: 668.3 nm ZP: -14.5 mV. PEG increased ZP and PS. The results were supported by TEM.

Conclusions: This study demonstrates that Ab-PEG-MOF can be efficiently produced, and Tamoxifen can be successfully loaded into this DDS.

Acknowledgements: This study was supported by TÜSEB under grant number 32590.

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P077
PREPARATION AND EVALUATION OF GELATIN/ALGINATE-BASED INKS FOR 3D PRINTING OF BONE SCAFFOLDS

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Introduction: 3D printing is one of the technologies widely used in tissue engineering and regenerative medicine to develop complex tissue structures to biomimicry organs and tissues (1). Sodium alginate enables bioprinting processes by providing high extrusion capacity and is a biocompatible material that ensures the stability of printed structures by rapid and irreversible cross-linking (2). Gelatin is a polymer used in the biomedical field due to its biocompatibility, lack of immune response in the body, degradability, and lack of toxicity (3). The aim of this study is to prepare sodium alginate/gelatin inks for 3D printing of biocompatible scaffolds to use in alveolar bone tissue engineering.

Materials and Methods: Ink formulations were prepared with different ratios of sodium alginate and gelatin. Viscosity measurements of ink mixtures were carried out with Brookfield rheometer. The pendant observation drop method was used to measure the surface tension of ink formulations. Young Laplace equation was used to calculate the surface tension values. The printability of ink formulations with 3D printing was evaluated. The formulations were printed layer by layer with 3D printing technology using 18G needle (Axolotl Biosytems, Türkiye). The printed formulations were crosslinked with 5% CaCl2 solution.

Results: As the amount of gelatin increased in the ink formulations, a decrease in viscosity values was observed. The surface tension values of inks were found to be approximately 50 mN/m. Ink formulations successfully printed with a 3D printer.

Conclusions: Sodium alginate and gelatin-based ink formulations were prepared successfully for 3D printing. Biocompatible scaffolds were obtained with the 3D printing technology and further studies are required to use scaffolds in alveolar bone tissue engineering. **Acknowledgements:** This study was supported by Gazi University Scientific Research Projects Coordination Office with guided project grant number TSG-2022-7922.

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P078
DEVELOPMENT AND IN VITRO EVALUATION OF SILK PROTEIN AND SPIRULINA MICROPARTICLES LOADED HYDROGEL FORMULATIONS.

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Introduction: Today, the cosmetic industry is focusing on researching more sustainable and effective active ingredients for skin care products. Silk protein is one of these substances; It is compatible with the skin, reduces water loss, moisturizes the skin, and increases elasticity (Daithankar et al. 2005). The natural active ingredient Spirulina, which is another good example in terms of sustainability, moisturizes the skin, prevents wrinkles, and has an anti-aging effect (Ragusa et al., 2021). In addition to these advantages, silk protein and spirulina have disadvantages such as bad odor, low stability, and low solubility. Silk protein and spirulina microparticles were prepared in our study to eliminate these disadvantages and extend the time the formulation stays on the skin and the duration of its effect. Then, the prepared microparticle system was dispersed in the hydrogel formulation, the formulation was given its final shape and evaluated under in vitro conditions.

Materials and Methods: All components were of analytical purity. First, incompatibility studies were carried out. Na-alginate microparticles were produced by the simple coacervation method and then loaded into chitosan hydrogel (2%). Critical process parameters were evaluated in the development studies of formulation. Detailed in vitro quality control studies were performed separately for microparticles and hydrogels.

Results: The microparticles were examined for particle size, zeta potential, surface morphology, appearance, and FT-IR parameters. Microparticle-loaded gel formulations were examined in terms of pH, rheology, and mechanical properties. As a result of in vitro studies, the optimum formulation was selected. The microparticle formulation was compatible with the literature in terms of the determined parameters. The optimum gel formulation showed suitable pH, mechanical and flow properties, typical gel-type mechanical spectrum (G' >> G") at 25 and 32°C Stability studies performed at 40°C/75%RH showed that the product retained its properties.

Conclusions: Our study aims to evaluate the use of silk protein and spirulina as cosmetics and the potential of new delivery systems and to contribute to the development of innovative approaches in skin care.

Acknowledgements: This study was supported by a grant from Ege University BAP (Project Number: 29728)

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P079
DEVELOPMENT OF AN OCULAR IN-SITU GEL FORMULATION CONTAINING INDOMETHACIN

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Introduction: Postoperative inflammation in the eye, frequently seen following cataract surgery. Non-steroidal anti-inflammatory drugs (NSAIDs) mostly used for controlling postoperative inflammation with the inhibition of the cyclooxygenase (1). Indomethacin (INDO), a topical NSAID is used in the treatment of the ocular inflammatory disorders such as conjunctivitis, uveitis, cystoid macular edema, and anterior segment inflammation, including post-operative pain following cataract surgery (2). In our study in-situ gel formulations were prepared for extended duration of INDO on the corneal surface which will improve the ocular bioavailability for sufficial treatment of ocular inflammatory disorders (3).

Materials and Methods: INDO was gifted by DEVA (Türkiye), Poloxamer® 407 (P407) was from Sigma (Germany). All other chemicals were in analytical grade. Formulations were prepared by cold method (4). Briefly polymers were dissolved in cold water and INDO was added to the solutions. A modified UV method was used. DSC, FT-IR and 1H-NMR analyses were used for the determination of structural properties of INDO. Characteristic properties of the formulations were evaluated by gelation temperature (GT) and gelation capacity (GC), pH, rheological analysis and in vitro drug release studies (pH 7.4 PBS at 34°C±2°C).

Results: According to the GT and GC analyses "IND-17" was selected for further studies (Table 1). DSC, FT-IR and 1H-NMR analyses of INDO were presented in Fig.1-Fig.3 respectively. INDO was loaded to the IND-17 formulation at 0.1% (w/w). pH of the formulation was 5.29 and considering the ocular tolerability no adjustment was required. The rheological analyses revealed the gel transition point at 34°C±2°C. Preliminary in vitro release analyses revealed that even after 6 hours only 30% of the INDO was released from the formulations showing the extended release of the active agent with the help of transition of the eye drops to the solidified gel structure.

Conclusions: It seems that ocular bioavailability will be enhanced with P407 based in-situ gels considering extended retention time of INDO on the corneal surface.

Acknowledgements: Indomethacin was gifted by DEVA (Türkiye). DOPNA-LAB (FT-IR analyses) and BIBAM (1H-NMR analyses) were acknowledged.

Table 1: Optimization of polymer concentrations

Code	P407 (%, w/v)	GT (°C)	GC (sec)
IND-12	12	40±2	1-2
IND-15	15	35±2	1-2
IND-17	17	34±2	1-2

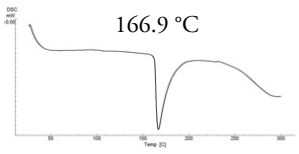

Fig.1. DSC

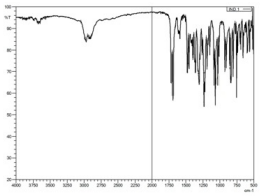

Fig.3. [1]H-NMR

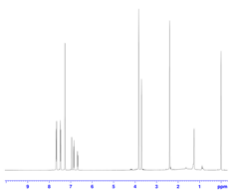

Fig.2. FT-IR

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P080
DEVELOPMENT OF CURCUMIN LOADED AQUASOMES BY USING CENTRAL COMPOSITE DESIGN

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Curcumin, derived from turmeric, has notable pharmacological advantages but suffers from poor bioavailability (1). This study explores the optimization of curcumin-loaded aquasomes—three-layered nanoparticles consisting of a hydroxyapatite core, carbohydrate coat, and the drug—using a Quality by Design (QbD) approach (2). The objective was to assess the impact of variables like drug amount, core-to-coat ratio, and incubation time on aquasome formulation.

The aquasomes were produced by forming a hydroxyapatite core, coating it with lactose, and loading the drug through adsorption. A Central Composite Design within Response Surface Methodology was employed to evaluate how these factors influence particle size, zeta potential, and polydispersity index (PDI) (3-5).

Results showed that a higher core-to-coat ratio generally resulted in a less negative zeta potential, implying reduced stability, although its effects on particle size and PDI were inconsistent. Longer incubation times were associated with smaller particle sizes and more negative zeta potentials, suggesting improved stability. Increasing the drug quantity tended to lower the zeta potential, potentially destabilizing the system, but had varying impacts on particle size and PDI.

Further characterization using Scanning Electron Microscopy and Energy-Dispersive X-ray Spectroscopy (EDX) confirmed successful aquasome formation, with typical hydroxyapatite elemental composition and evidence of curcumin adsorption altering surface properties.

The study concluded that adjusting incubation time and core-to-coat ratio is more crucial than altering drug quantity for optimizing curcumin delivery. The findings support aquasomes' potential as an effective carrier, for enhancing bioavailability and therapeutic effect, with Run 4 identified as the optimal formulation.

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P081
PREPARATION OF GARLIC AND LAVENDER OIL-CONTAINING NANOFIBERS VIA ELECTROSPINNING FOR THE TREATMENT OF ALOPECIA AREATA

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Introduction: Alopecia areata, is an autoimmune, inflammatory, organ-specific disease characterized by the loss of hair in areas of the body where hair is normally present, such as the scalp, beard, eyelashes, and eyebrows. Garlic essential oil, rich in sulfuric compounds reported to have many beneficial medicinal effects including hypotensive, anti-tumor, antimicrobial, immunomodulatory, and hair growth effects, is used in the treatment of alopecia (1). The antimicrobial properties of garlic essential oil help to eliminate fungi and bacteria that can damage the scalp and suppress hair growth. Lavender (Lavandula angustifolia), due to its high yield and quality of essential oil, is an important medicinal, cosmetic, and perfume plant cultivated worldwide and beneficial for hair growth. In this project, nanofiber formulations containing garlic and lavender essential oils have been produced.

Materials and Methods: Lavender and garlic oils were purchased from Ongen Medikal. Cellulose acetate (5%) and Eudragit S100 (10%) containing polymer solutions were prepared in different ratios (10:0, 9:1, 8:2, 7:3 of acetone: dimethylacetamide (DMAC) with 100 µL of lavender and 100 µL of garlic oil), and nanofibers were fabricated via electrospinning method. Viscosity, conductivity, and surface tension values of the polymer solutions were measured. The morphology and mean diameter of nanofibers were evaluated with SEM images of nanofibers. In addition, mechanical (tensile strength and elongation at break) and wettability properties of nanofibers were analyzed.

Results: The addition of DMAC to the polymer solution did not affect the conductivity and surface tension values. Besides, the viscosity values decreased with the addition of DMAC and were found between 71,57-127,23 cps. All polymer solutions containing garlic and lavender oil electrospun continuously with process parameters of 16-20 kV voltage, 15-17 cm distance and 0,8 mL flow rate. The mean diameters of nanofibers were found between 98-140 nm according to SEM images. The addition of DMAC increased the mechanical properties of the nanofibers. Nanofibers containing DMAC exhibited higher tensile strength and elongation at break values. The wettability studies indicated that all formulations had hydrophobic surface characteristics due to high contact angle values (>130°).

Conclusions: Garlic and lavender oil containing nanofibers were fabricated successfully. The undesirable odor of garlic oil hindered with the lavender oil. Further studies are needed to show the effectiveness of nanofiber formulations on the alopecia treatment.

Acknowledgments: This study was supported by a grant from The Scientific and Technological Research Council of Turkey (TUBITAK 2209-A Research Project Support Programme for Undergraduate Students, 1919B012301400).

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P082
EVALUATION OF CHITOSAN-COATED NANOLIPOSOMES CONTAINING VARDENAFIL FOR PULMONARY ARTERIAL HYPERTENSION

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Introduction: Pulmonary arterial hypertension (PAH) is a disease characterized by pulmonary vascular remodeling, increased pulmonary arterial pressure, and pulmonary vascular resistance in small pulmonary arteries1. In healthy individuals, the right ventricle pumps dirty blood to the lungs through the pulmonary arteries for oxygenation, but when the disease develops, these vessels narrow. In PAH, progressive increase in pulmonary vascular resistance, decrease in pulmonary vascular compliance, and increased pulmonary artery pressure result in right heart dysfunction and death2. Vardenafil is a phosphodiesterase-5 (PDE5) inhibitor and shows its effect through the nitric oxide (NO) pathway. Vardenafil reduces cGMP hydrolysis by inhibiting PDE5, and increased cGMP levels provide smooth muscle relaxation3. Studies have shown that vardenafil can cause vasodilation in the pulmonary vessels much more effectively compared to other PDE5 inhibitors. It is thought that the oral bioavailability of vardenafil can be increased by extending its half-life with a suitable drug carrier system.

Materials and Methods: Vardenafil-loaded nanoliposomes were prepared by ethanol injection method using phosphatidylcholine and cholesterol. The same formulation was also prepared by coating with chitosan. Particle size, polydispersity index, and zeta potential of the nanoliposomes were measured. In vitro dissolution studies of the prepared nanoliposomes were carried out by dialysis method in pH 1.2 environment for 8 hours and the results were compared.

Results: As a result of the comparison of chitosan-coated (273.4 nm) and uncoated nanoliposome (101.7 nm) formulations, an increase in the particle sizes of chitosan-coated nanoliposomes was observed. While vardenafil release from uncoated nanoliposomes was 70%, chitosan-coated nanoliposomes released 28% after 8 hours in in vitro dissolution studies.

Conclusions: Chitosan-coated nanoliposomes have been observed to delay the release of vardenafil. These results suggest that vardenafil may increase bioavailability by extending its duration of action.

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P083
IN-SITU GEL FORMULATION WITH ANTI-INFLAMMATORY EFFECT FOR PREVENTING ALVEOLAR OSTEITIS AND ORAL WOUNDS

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Introduction: "Alveolar osteitis" (AO) is a common condition observed after dental procedures or tooth loss, characterized by recurring and severe pain. The aim of this study is to prepare thermosensitive gel formulations incorporating dexketoprofen trometamol (DKT), which provides effective analgesia in acute postoperative pain.

Materials and Methods: Formulations prepared with varying concentrations of GP, CS, and NaHCO3. 2% CS was added to 0.1 M acetic acid solution. GP was dissolved in 0.1-0.3 M NaHCO3 solution. Finally, DKT was added in a ratio of 1.25% to the GP solution and then two solutions were mixed. The gelation temperature and time were determined using oscillation measurements with a rheometer (TA-TX Discovery HR 1 Instruments, UK), equipped with a plate and plate combination (diameter 40 mm, with the gap of 1 mm) (Rossi et al., 2010). The in-vitro release profiles were obtained using dialysis tubing release immersed in 100 mL of phosphate buffer (pH 6.8) under sink conditions at 37°C±0.5°C, stirring at 200 rpm continuously (Adısanoğlu & Özgüney, 2024). Samples were analyzed spectrophotometrically.

Results: The gelation temperature of the formulations were determined between 26 and 40.1°C, the chosen optimal formulation exhibits a gelation temperature of 36.2°C. Gelation time of this formulation was determined as 4.3±0.262 min. In-vitro release studies showed that the formulation released 99% of drug in 8 hours.

Conclusions: To prevent the dislodging of the formed blood clot and provide a barrier between the oral environment and the wound, the developed formulation could be a promising candidate for the treatment of AO.

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P084

ENHANCED OCULAR DELIVERY OF VORICONAZOLE UTILIZING POLYMERIC NANOPARTICLES: A PROMISING STRATEGY FOR TREATING FUNGAL KERATITIS

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Introduction: Fungal keratitis is a severe infectious corneal disease (1). Voriconazole is a second-generation triazole agent with a broader spectrum compared to other azole antifungal drugs (2). Providing an effective dose with conventional ocular drug delivery systems is quite difficult due to the special anatomical, physiological and biochemical structure of the eye. Polymeric particulate ocular drug delivery systems increase bioavailability with advantages such as extending the residence time of the drug in the eye, controlled drug release and targeting (3). Therefore, in this study voriconazole loaded polymeric particles were formulated.

Materials and Methods: Voriconazole (VOR) (gifted by Deva İlaç, Türkiye), Polycaprolactone (PCL) (Sigma-Aldrich, Germany), Eudragit FS 100 (FS 100) (Evonik, Germany). All other chemicals were in analytical grade. Spray drying method was used for the preparation of particles. Particle size (PS), polydispersity index (PDI) and zeta potential (ZP) analyses (Malvern Zetasizer, UK), SEM (Zeiss Ultra Plus FE-SEM, Germany), FT-IR (IR Affinity-1S Shimadzu, Japan), DSC (DSC-60, Shimadzu USA) and 1H-NMR (Fourier 300 NMR Bruker, USA) analyses, Voriconazole amounts and in vitro release studies were performed.

Results: Compositions, PS, PDI, ZP, Voriconazole amounts (Table 1), SEM analysis (Fig. 1) DSC (Fig. 2), FT-IR (Fig. 3), 1H-NMR (Fig. 4), in vitro release analyses results (Fig. 5) and were presented.

Conclusions: According to the analyses results PCL-FS-100 particles are promising candidate for the ocular applications of VOR for the treatment of fungal keratitis.

Acknowledgements: DOPNA-LAB for FT-IR, BIBAM for Spray Dryer, 1H-NMR and SEM Analyses

Table 1. Compositions and PS, PDI, ZP, Voriconazole amount analyses results of the particles (n=3)

Code	VOR (mg)	PCL (g)	FS100 (g)	PS (nm)	PDI	ZP (mV)	VOR (%w/w)
SPEV-1	50	1	1	84,73	0,283	-1,12	1,76 ± 0,44
SPEV-2	100	1	1	84,39	0,481	1,55	4,50 ± 0,38
SPEV-3	150	1	1	201,1	0,517	0,675	6,03 ± 0,55

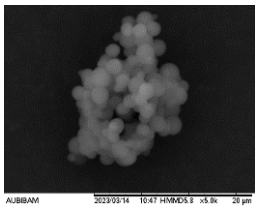

Fig.1 SEM

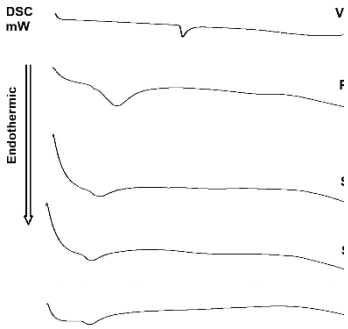

Fig.2 DSC

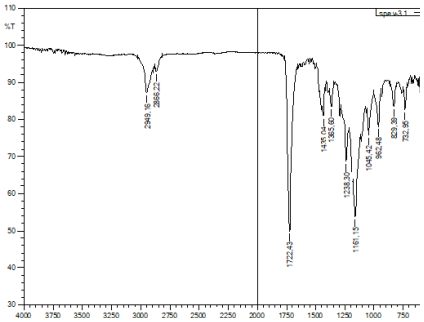

Fig.3 FT-IR

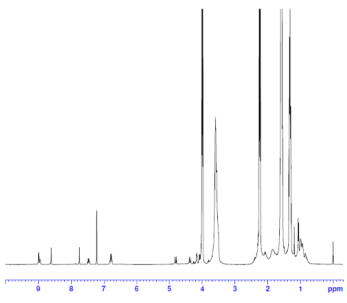

Fig.4 ^{1}H-NMR

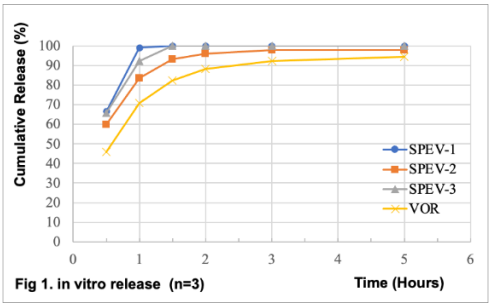

Fig.5 *In-vitro* Release

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P085
PREPARATION AND CHARACTERIZATION OF OLANZAPINE LOADED NANOSPONGES

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Introduction: Olanzapine, a poorly water-soluble antipsychotic drug, possesses significant challenges in formulation development due to its limited solubility and poor bioavailability (1). Nanosponges exhibit unique properties such as high loading capacity, tunable pore size, and biocompatibility, making them ideal for drug delivery (2). This study presents a method for enhancing olanzapine delivery through Nanosponges, which were characterized using techniques like zeta potential, particle size, scanning electron microscopy (SEM), Fourier-transform infrared spectroscopy (FTIR), and differential scanning calorimetry (DSC). The nanosponges' encapsulation efficiency and drug loading ability were also assessed for drug delivery applications.

Materials and Method: Four formulations were prepared using emulsion solvent diffusion, with olanzapine and ethylcellulose in dichloromethane slowly added to a definite amount of PVA and poloxamer 188 in aqueous continuous phase. The mixture was homogenized at 14000 rpm for 30 minutes and 1500rpm on magnetic stirrer for 30 minutes. The formed olanzapine nanosponges were dried in an oven at 40^{0}C for 48 hours (3)

Results: The study found that olanzapine successfully encapsulated within a nanosponge matrix, with particle sizes of 130nm and 158nm for blank and loaded nanosponges, respectively. The zeta potential values were -27mV and -32mV for blank and olanzapine loaded nanosponges, respectively. SEM analysis revealed the formation of spherical nanosponge particles with a porous structure, conducive to drug entrapment. The FTIR spectra showed stable character of olanzapine in mixture of polymers. DSC study revealed that drug engaged in binding with nanosponges.

Conclusion: Overall, this study offers valuable insights into the preparation and characterization of olanzapine Nanosponges as the physicochemical properties of the nanosponges were found to be suitable for oral drug delivery applications and it highlights the potential of nanosponges as effective carriers for improving the therapeutic efficacy of olanzapine.

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P086
DEVELOPMENT OF A POLYESTER BASED THERMO-RESPONSIVE HYDROGEL FORMULATION FOR DICLOFENAC SODIUM DELIVERY

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Introduction: Numerous people suffer from rheumatoid arthritis worldwide and the prevalence of rheumatoid arthritis increases each year, which has a significant negative impact on society. Rheumatoid arthritis (RA) is an autoimmune and chronic inflammatory disorder that decreases the quality of life (1). Hydrogels, composed of water and polymer frameworks, are ideal for delivering drugs or cell treatments to joints, allowing modified-release and healing of damaged tissue (2). The goal of this study is to develop and characterize diclofenac sodium-loaded thermo-responsive injectable hydrogel formulation.

Materials and Methods: Within the scope of the study, poly(ethylene glycol)-block-poly(ε-caprolactone)-block-poly(ethylene glycol) (PEG-PCL-PEG) thermo-responsive triblock copolymer was synthesized to formulate diclofenac sodium within a thermo-responsive hydrogel. The triblock copolymer was synthesized via ring-opening polymerization method. PEG-PCL-PEG polymer was characterized using 1H-NMR, FTIR, and GPC analyses. Diclofenac sodium was formulated using this polymer to obtain thermo-responsive hydrogel. The developed hydrogel was characterized by a drug release profile, thermal gelation point analysis, rheology, and viscosity analyses.

Results: The results of 1H-NMR, FTIR, and GPC analyses show that the PEG-PCL-PEG polymer was synthesized successfully with a narrow PDI value. Diclofenac sodium bearing PEG-PCL-PEG hydrogel showed a physical transition from solution to gel form around 37°C. The rheological properties and release profile showed that the developed hydrogel formulation would be an appropriate candidate for parenteral application which needs further in-vivo tests.

Conclusions: The results show that we have developed a suitable diclofenac sodium-loaded PEG-PCL-PEG thermo-responsive hydrogel for rheumatoid arthritis.

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P087

STRAT-M® - TRANSDERMAL DIFFUSION TEST MEMBRANE: IN-VITRO PERMEATION STUDIES WITH DIFFERENT PENETRATION ENHANCERS

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Introduction: Caffeine, an alkaloid compound, can promote hair growth, slow down the skin aging caused by UV radiation, and reduce cellulite by breaking down fat cells and improving blood circulation. This alkaloid is frequently used as hydrophilic model substance for human and animal skin permeation studies using Franz Diffusion cell with different synthetic membranes. This study aims to investigate the correlation between the in vitro permeation behavior of topical formulations through a transdermal diffusion test membrane (Strat-M® EMD Millipore, MA) and the classical regenerated cellulose membrane in the presence of Transcutol® and Tween 80® as penetration-enhancers. Strat-M® offers consistency, accessibility, and minimal variability for skin permeation studies in comparison with monolayer membranes (1).

Materials and Methods: 2% caffeine was used as a model active substance in 1% Carbopol 934® gels. Either Transcutol® or Tween 80® were added as enhancers in a ratio of 2%. Formulations were characterized in terms of viscosity, pH, mechanical properties and content uniformity. Then, in vitro permeation studies were carried out using Franz diffusion cells and caffeine amount were analyzed spectrophotometrically.

Results: The pH values of each formulation were compatible with the skin pH and their textural properties and viscosities were found suitable for topical application. Besides, content uniformity results show that caffeine was dispersed homogeneously into the gel formulations. 3.75% and 2.55% caffeine were found in receptor compartment when Strat-M® was used, while 45.30% and 46.9% caffeine release from regenerated cellulose membrane was observed for the gel formulations prepared using Tween 80 and Transcutol®, respectively.

Conclusions: As a result of this study, it was concluded that Strat-M® mimics the structure of skin better than classical synthetic membrane. There was no significant change in the pH and viscosity of the formulations as a result of two-month stability studies.

P088
DEVELOPMENT OF DUAL-MEDIATED LIPOSOMAL SYSTEMS

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Introduction: Liposomes are spherical drug carrier systems consisting of a bilayer of phospholipids with sizes varying between 30nm -1mm. Due to the amphiphilic property of phospholipids, both hydrophilic, hydrophobic and amphiphilic drugs can be loaded into liposomes. Liposomes can provide co-delivery of multiple drugs in a single formulation and are used as a dual drug release tool (1). This approach is especially preferred in case of treatments that require the synergistic action of two drugs. Acyclovir, an antiviral active ingredient, is used in varicella-zoster and herpes simplex virus infections. However, one of its drawbacks is nephrotoxicity in the kidneys as it is the main excretion route. One of the strategies that aim to reduce the toxicity of acyclovir is to give it in combination with curcumin (2). The current study is focused on the formulation of these two active molecules in liposomal carriers which can be used to reduce acyclovir nephrotoxicity.

Materials and Methods: Soy lecithin, cholesterol, acyclovir, and curcumin were dissolved in methanol. The solvent was evaporated in the evaporator to obtain a thin film. The resulting thin film was hydrated in ultrapure water using a vortex. It was sonicated using a probe sonicator for 5 minutes in 9 cycles at 50% power.

Results: The particle size and zeta potential of the prepared liposomal formulations were analyzed. The particle size of the empty liposome was found to be 117 .4 nm, zeta potential was -56.8 mV. While the average particle size of the liposome formulation containing curcumin and acyclovir was found to be 134.7 nm, average zeta potentials were also found -20mV. The increase in particle size and change in zeta potential are some of the findings indicating that the active substance is loaded into the liposome. A UV-spectrophotometric analytical method was developed to measure the amount of curcumin and acyclovir. The lmax for acyclovir was 254 nm while curcumin gave absorbance at 262nm and 424nm. Due to this wavelength overlap, the encapsulation efficiency was determined using derivative spectrophotometry.

Conclusions: This study shows that curcumin and acyclovir are loaded into the liposomes. The nephrotoxicity caused by acyclovir could be reduced by giving these two active substances in a single liposomal formulation.

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P089
ENCAPSULATION OF PROBIOTIC BACTERIA USING MICROFLUIDIC CHIP SYSTEM FOR ULCERATIVE COLITIS TREATMENT

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Introduction: Probiotic bacteria can play an important role in the treatment of ulcerative colitis (UC) by improving the barrier function of the intestine (1). It is thought that practices that restore a stable intestinal microbiota to achieve and maintain UC remission may be safe and effective as a complementary therapy (2). In general, there are many methods for cell encapsulation. However, many techniques have limitations such as reproducibility, ease of production, variable size distribution and non-uniform morphology (3). It is crucial that the technique chosen for encapsulating probiotics does not compromise the viability of encapsulated cells and provides mechanical stability suitable for the intended application (4). This study focuses on the development of a probiotic encapsulated drug delivery system using microfluidic technology for the treatment of UC.

Materials and Methods: Probiotic bacteria were produced by incubating them in MRS broth sterile liquid medium at 37oC in an oven for 48 hours. Probiotic bacteria were purified from the medium by centrifugation and dispersed with PBS solution. To prepare W/O emulsion systems, this dispersion was used as the aqueous phase and melted solid lipid with a melting point of 34-38 °C was used as the oil phase. MB5-Z500 microfluidic chips were selected to build the microfluidic system. The obtained emulsions were collected in enteric capsules and lyophilized. The viability and survival rates of microencapsulated bacteria were checked.

Results: As a result of in vitro tests conducted on the final product, it has been determined that the encapsulated bacterium can reach the intestinal environment without being affected by the negative effects of the gastrointestinal system.

Conclusions: It has been determined that the developed enteric capsules are effective in preserving the viability of bacteria and it has been shown that their use in the treatment of UC may be possible.

Acknowledgements: This study was supported by a grant of Anadolu University Coordinator of Scientific Research Projects (Project ID: 117)

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P091
DEVELOPMENT OF PRONIOSOMAL DRY POWDER INHALER FORMULATIONS USING DIFFERENT METHODS

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Introduction: Proniosomes are dry powder formulations created from non-ionic surfactants and water-soluble carrier particles. When exposed to water or biological fluids, proniosomes convert into niosomes (1). Proniosomes can potentially enhance pulmonary drug delivery by improving the flow and distribution of drugs (2). This study explores the development of proniosomal dry powder inhaler formulations for targeting the lungs, using various methods and optimizing aerodynamic particle size.

Materials and Methods: In this research, proniosome formulations without active pharmaceutical ingredients (API) were prepared using the slurry and thin film-hydration methods. Inhalation-grade lactose, Lactohale LH 300, supplied by DFE Pharma, served as the water-soluble carrier. Span 60, a non-ionic surfactant from Sigma Aldrich, and cholesterol from Amresco were used to form the niosome structure. Magnesium stearate (MgSt) from Sigma Aldrich was added to the formulation to prevent aggregation. A Buchi rotavapor was employed for the slurry and thin film hydration methods, and a Teknosem lyophilizer was used for lyophilization. Ultrasonic bath, vortex, and probe-sonicator techniques were applied to reduce particle size. The resulting dry powder formulations were sieved using 200 mesh (77 µm) sieves. Particle size analysis of the proniosomes was conducted using laser diffraction with the Sympatec Helos H0728 device, calculating Dv10, Dv50, Dv90, and span values. Niosome particle size, polydispersity index (PI), and zeta potential were measured using a Malvern Zetasizer Pro.

Results: The average proniosome particle size (Dv50) for formulations produced via the slurry and thin film hydration methods was approximately 5 µm. Niosome particle sizes ranged from 1 to 3 µm, with PI values between 0.200-0.500 and zeta potential values below -40 mV. Results from measurements with the New Generation Impactor (NGI) device will be included.

Conclusions: Laser diffraction measurements showed that the dry powder formulations have particle sizes suitable for inhalation. Prototype blank formulations, to which APIs can be added, have been successfully prepared. The study concludes that further optimization will be more straightforward after incorporating the API.

Acknowledgements: This study was supported by Ankara University Scientific Research Projects Commission under the grant no: TDK-2024-3297.

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P092
CHITOSAN-POLYVINIL ALCOHOL BASED ORAL HYDROGEL FORMULATIONS FOR COLON TARGETING

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Introduction: Stimuli sensitive hydrogel drug delivery systems are very applicable in pharmaceutical area due to their physical characteristics that change in response to external stimuli. The swelling or shrinking of pH-sensitive hydrogels due to pH change throughout the gastrointestinal tract controls drug release, making them suitable for targeting to the colon (1). The aim of the present study is to develop a pH-sensitive oral hydrogel formulation to deliver the model drug, dexketoprofen trometamol to the colon.

Materials and Methods: pH-responsive colon targeted oral hydrogel formulations were prepared by mixing the chitosan and PVA solutions at a certain concentration and cross-linking with glutaraldehyde (2). The formulations were optimized by varying chitosan:PVA ratios and glutaraldehyde amounts. The colon targeted hydrogels were characterized in terms of drug content, pH value, mechanical properties, swelling behavior, and in vitro dissolution rate of dexketoprofen trometamol.

Results: In this study, colon targeted drug delivery formulations of dexketoprofen trometamol, were developed. It has been noted that varying the cross-linker concentration and polymer ratios have a major impact on the mechanical properties, swelling behavior. In vitro drug release characteristics of the developed hydrogel based formulations were found to be effected in response to pH change.

Conclusions: The designed pH-sensitive oral hydrogel formulation of dexketoprofen trometamol demonstrated physicochemical properties appropriate for oral administration, and sustained drug release, and presents a promising approach for colon targeting.

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P093
ANTIBIOTIC LOADED THERMOSENSITIVE HYDROGEL FORMULATION FOR OTITIS MEDIA TREATMENT

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Introduction: Otitis media (OM) is one of the most commonly treated childhood diseases in the world. Considering the clinical studies of OM treatment, locally applied hydrogel systems that can provide controlled and long-term drug release are promising. Hydrogels can be used as sustained-release depot drug delivery systems for non-invasive transtympanic treatment of OM (1). Within the scope of this study, thermosensivite hydrogel formulations containing ciprofloxacin HCl were designed as a drug delivery system that will provide sustained drug release for the treatment of OM.

Materials and Methods: Thermosensitive hydrogel formulations based on poloxamer were prepared by cold method (2). Poloxamer 407 (P407) solutions at certain concentrations were prepared and cooled to 4 °C. For chitosan-poloxamer hydrogels, chitosan solutions at 4°C were used as solvent for poloxamer. The drug content, pH, viscosity, mechanical properties, gelation temperature and duration, and swelling behavior, and in vitro dissolution rate studies were carried out.

Results: Based on the appropriate properties such as 32.8±0.84 C° gelation temperature and 2.5±0.38 min gelation time, 16% (w/v) P407 was selected as a thermosensitive gelling agent. Then the effect of the addition of three different concentrations of chitosan to hydrogels was investigated. In accordance with the target properties, hydrogel formulation containing 1% (w/w) chitosan, with drug content above 98%, which can form gel at 34.9±0.26 C° and in 3.8±0.34 min, and shows sustained drug release compared to the free drug were obtained.

Conclusions: The developed thermosensitive hydrogel formulation offers a promising method for the local treatment of OM.

Acknowledgments: This study was supported by a grant of TUBITAK 2209-A

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P094

THE EFFECT OF COMBINED POLYMER USAGE AND NUMBER OF LAYERS ON THE CHARACTERIZATION OF 3D PRINTED METRONIDAZOLE-LOADED PERIODONTAL FILMS

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Introduction: In this study, periodontal films loaded with metronidazole (MNZ) were produced by 3D printing with Semi-solid extrusion method (1), since it is very important to apply personalized doses according to the depth of the periodontal pocket. The aim of this research was evaluating the effect of the use of combined polymers and the number of different polymer layers on formulation characterization. While chitosan was preferred in the formulation due to its non-toxicity, antimicrobial, anti-inflammatory, tissue regeneration activities, biodegradability, virucidal and fungicidal effects, bioadhesiveness, alginate was preferred due to its high-water retention capacity, biocompatibility, and low toxicity. MNZ was preferred because of its specific activity against various anaerobic bacteria, as it is a widely used antibacterial agent for periodontitis.

Materials and Methods: MNZ-loaded chitosan gels were prepared by dissolving chitosan and MNZ in 1.5% (v/v) acetic acid. Propylene glycol was used as plasticizers. MNZ-loaded alginate gels were prepared by dissolving alginate and MNZ in distilled water. Calcium chloride was used as crosslinker for alginate gel. Films were printed by an Axo A1 3D printer (Axolotl, Turkey) within 10 layers for all formulations, but the number of chitosan and alginate layers contained in the films from top to bottom was different (F1(10C), F2(10A), F3(3C4A3C) and F4(1C3A2C3A1C)). Thickness, adhesiveness, mechanical strength, degree of swelling and in vitro drug release were evaluated (2).

Results: The highest thickness were found at chitosan film (F1) (231.67µm±8.16) while F2 (alginate) had lowest thickness (100.55µm±2.51). The highest adhesiveness was obtained by F2 (2.79N±0.08). However, adhesiveness decreased ((0.15N±0.21 for F3 and 0.47N±0.19 for F4)) when chitosan was placed at the bottom and the top of the film. While the highest tensile strength was obtained by F1, by combining chitosan and alginate, the lowest one was obtained by F3 (from 14.78 MPa±4.34 to 4.31 MPa±0.82). The highest swelling degree was detected at F4 (863.07%±45.05). While F2 dissolved 100% in 5 minutes, it was observed that the released amount of MNZ increased from 41.67% to 88.63% in 240 minutes depending on number of alginate layers.

Conclusion: This study showed that the use of combined polymers and the number of polymer layers were effective on the characterization of films prepared by 3D printing. MNZ release can be modified by using different type of polymers with different number of layers.

Acknowledgements: This study was supported by a grant of TUBITAK (2209-A)

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P095

COMPARATIVE EVALUATION OF THE ANTIFUNGAL ACTIVITY OF TOPICAL GELS CONTAINING TEA TREE, THYME AND CLOVE ESSENTIAL OILS

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Introduction: Fungal skin infections are a common and serious global health issues. Current treatment options have limitations such as the high toxicity of antifungal agents, the effects of pharmacodynamic-pharmacokinetic mechanisms, and the occurrence of antifungal resistance. Essential oils from various plants are natural resources that have been used in modern and traditional medicine for centuries as antifungal and antimicrobial agents. In this study, gel formulations of tea tree oil, thyme oil and clove essential oils were prepared and their antifungal activities on T. rubrum, M. canis, and C. albicans strains causing skin fungal infections were investigated comparatively.

Materials and Methods: Formulations containing each of the essential oils (Nuka, Turkey) (0.5%) and a placebo were prepared. Carbomer (1%) was kept in a sufficient amount of distilled water overnight as a gelling agent. Polysorbate 20 (0.5%) was used as surfactant and glycerin (2%) and d-pantenol (2%) were used as emollients. 0.2% EDTA was used as chelating agent and Sensiva as preservative. After mixing the other ingredients in the formulation for gelling of carbomer, TEA was added in sufficient quantity to adjust the pH. The gels were then characterized according to pH and viscosity values and their antifungal activity was evaluated comparatively.

Results: The MIC values of the gels prepared with essential oils were evaluated according to the CLSI accuracy range. The gel formulation containing 0.5% thyme essential oil showed significant efficacy against placebo in clinical isolates of C. albicans and T. rubrum. The gel formulation containing 0.5% clove oil showed twice the efficacy of placebo in clinical isolates of C. albicans. The gel formulation containing 0.5% tea tree oil showed no significant efficacy.

Conclusions: The gels developed in this study have optimal pH and good rheological properties suitable for topical application. The essential oil gel formulations showed significant antifungal activity for the microbiological isolated used. It is predicted that this gel formulation with natural components may be effective and alternative in the treatment of skin fungal infections in humans.

Acknowledgements: This study was supported by Scientific Research Project Coordination Unit of Istanbul University (Project Number: 34079)

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P096
DESIGN AND IN VITRO CHARACTERIZATION OF NIOSOMES LOADED WITH VITAMIN C

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Introduction: Vitamin C (ascorbic acid-AA) is one of the essential vitamins responsible for various chemical reactions in the human body. It is an antioxidant substance that reduces free radicals, which can pose a risk of various diseases. It acts as a cofactor in biochemical activities. Humans cannot synthesize Vitamin C endogenously; thus, they need to obtain it from foods or dietary supplements (1). The pharmacokinetics data of AA points to a variable bioavailability profile. Thus, there is a need to develop stable drug delivery systems that enhance its bioavailability and pharmacokinetics while prioritizing degradation. Niosomes, which are vesicles with a bilayer structure prepared with non-ionic surfactants similar to liposomes, are considered a better option due to their better chemical stability profile and the ability to modify their surface properties. This study aims to prepare niosomes containing the derivatives of C vitamin and characterize them in vitro (2).

Materials and Methods: The niosomes loaded with AA, sodium ascorbate (NaA), and ascorbyl palmitate (AP) were prepared using surfactants such as Brij 76, Span 20, and Span 40 by the thin film hydration method (3). The niosomes obtained, were characterized regarding entrapment efficiency (EE%), particle size, zeta potential, in vitro dissolution profiles, and interaction between drug-excipients.

Results: The particle size of the lyophilized niosomes entrapped NaA was between 1,061- 4,95 µm, and the zeta potential was -56 mV. AA could not be loaded in niosomes, while the EE% of NaA loaded into lyophilized niosomes prepared with Brij 76 was 18,20; 90,8% of NaA was released from lyophilized niosomes in simulated gastric fluid (pH 1.2) at 90. min. The particle size and zeta potential of lyophilized Span 40 niosomes containing AP were 0,992-1,774 µm and -22,1 mV, respectively. AP was loaded completely into liposomes.

Conclusions: The study's findings revealed that ascorbic acid, due to its high aqueous solubility, could not be effectively entrapped in a vesicular system. However, the derivatives with lower aqueous solubilities, such as NaA and AP, were successfully loaded into niosomes. This success paves the way for the evaluation of niosomes NaA and AP as a drug carrier system with high bioaccessibility for oral administration, as well as an antioxidant food additive.

Aknowledgements: This study was supported by a grant of TUBITAK (2209-A TÜBİTAK - BİDEB)

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P097
INVESTIGATING THE IMPACT OF CROSS-LINKER TYPE ON PARTICLE SIZE AND ZETA POTENTIAL OF ALBUMIN NANOPARTICLES

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Introduction: To optimize the passive targeting of nanoparticles to the diseased area, it's crucial to take into account the size of the particles. In the present study, we aimed to define the cross-linker to be used to obtain the targeted particle size and zeta potential of Bovine Serum Albumin nanoparticles by using three different cross-linking agents.

Materials and Methods: Bovine albumin and glutaraldehyde was obtained from Sigma-Aldrich, 1-ethyl-3-(3-(dimethylaminopropyl)-carbodiimide (EDC) was obtained from Thermo Fisher, USA , Genipin was purchased from ABCR. 1,6% glutaraldehyde solution in water, 0,01 mg/ EDC in water and % 0,1 m/V genipin in DMSO was used as the cross-linker. Nanoparticles of different cross-linkers were compared by measuring final particle size, polydispersity index, and zeta potential. Encapsulation efficiency was measured by indirect method using UV spectrophotometer.

Results: Results are shown in Table 1.

Table 1: Particle size, polydispersity index, and zeta potential of BSA nanoparticles prepared with different cross linkers

Drug substance-Cross linker type	Particle size	PDI	Zeta Potential	Encapsulation efficiency (%)
DS1-GLU	109,5 ± 1,053	0,088 ± 0,009	-38,05 ± 1,842	70,1
DS2-GLU	104,5± 1,617	0,087± 0,018	-39,43± 2,665	61,15
DS1-EDC	182,3 ± 1,156	0,043 ± 0,029	-27,6 ± 0,432	60,3
DS2-EDC	165,2 ±1,678	0,150 ± 0,049	-27,76 ±1,082	56,78
DS1-Genipin	159,7 ± 1,292	0,214 ± 0,011	-41,21 ± 1,482	53,9
DS2-Genipin	126,2± 0,147	0,252 ± 0,022	-39,56 ± 0,879	66,3

Conclusions: Particle size of 100-200 nm has an effective ability to target the inflamed synovium (1, 2). In terms of particle size and zeta potential, optimal formulation parameters were defined for all the cross-linkers. The polydispersity index (PDI) was found to be lower than 0.3, indicating a narrow nanoparticle size distribution. If conjugation is needed, lower nanoparticle size can be preferred.

Acknowledgements: This study was supported by a grant of TÜSEB (TÜSEB-24330-B Grubu)

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P098
STIMULI-RESPONSIVE FIBERS FOR SKIN TISSUE ENGINEERING

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Introduction: In tissue engineering, scaffolds are used to simulate the extracellular matrix in order to enhance the regeneration of injured tissues (1). Different factors can improve cell proliferation and therefore four-dimensional (4D) scaffolds, which are 3D platforms that react to external stimuli, have been developed (2). In this scenario, electrical stimulation has attracted attention. Polypyrrole is an electrically conductive polymer and has been described as able to promote the passage of electrical current (3).

Given these premises, the aim of the present study was the design and the manufacturing of 4D scaffolds based on polycaprolactone (PCL) and zein (Z) fibers, coated with polypyrrole (PPy), via electrospinning, to promote skin regeneration.

Materials and Methods: PCL-Z blends in a ratio 10:1 were prepared in acetic acid 96% v/v and subjected to electrospinning.

Fibers morphology and diameters were evaluated by means of the scanning electron microscope. Mechanical properties were assessed on both dry and hydrated samples. Preliminary results of scaffolds biocompatibility on normal human dermal fibroblasts were collected.

Afterwards, the fibrous scaffolds were coated with different loadings of PPy. Fibers were immersed into an acqueous solution containing pyrrole in a range from 0.015 M to 0.09 M. Then pyrrole was allowed to polymerize by adding an aqueous solution of $FeCl_3$ in a range between 0.03 M and 0.18 M as an oxidant agent.

Results: PCLZ fibers were easily obtained via electrospinning. Regular and homogeneous nanofibers have been collected with a mean diameter of 490 nm. In terms of mechanical properties, no statistically significant changes in the values of force at break point were observed between PCL and PCLZ.

Moreover, scaffolds can be considered biocompatible as shown by the preliminary results.

The polymerization of pyrrole was successful when using a concentration of pyrrole and $FeCl_3$ concentration above 0.03 and 0.06, respectively, as it is observed that, at these concentrations, the color of the scaffolds turned from white to black in color. SEM images show that PPy particles adhere to the fiber surface.

Conclusions: The study allowed to successfully develop PCLZ fibers via electrospinning. Preliminary results show that PCL-Z fibers, coated with PPy, can be produced. Further studies are on-going to evaluate the impact of the coating on the scaffolds mechanical properties and biocompatibility.

Acknowledgments: This work was partially funded by Horizon Europe project FORCEREPAIR - "Smart and multiFunctional 3D printable prO-Regenerative biologiCal matrix modulating mEchanotRansduction as advancEd theraPy to treAt skIn chRonic wounds" under the grant agreement No. 101092243

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P099
CENTRIFUGAL SPUN MICROFIBERS FOR THE TREATMENT OF SKIN CHRONIC WOUNDS

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Introduction: Non-healing skin chronic wounds exhibit a disrupted healing process which holds them in a self-perpetuating inflammatory state1. Centrifugal spinning is making its way as an advantageous fiber production method to obtain 3D scaffolds to stimulate skin reparation2. Clay minerals like layered double hydroxides (LDH) are promising additives due to their interesting properties3. Therefore, the aim of this work was the development of centrifugal spun microfibers based on polyvinylpyrrolidone (PVP) and polylysine (PLL) doped with LDH based on Mg and Al intercalated with gallic acid (GA) to produce antibacterial and antioxidant scaffolds.

Materials and Methods: Pristine and GA-intercalated MgAl LDH were synthesized using the coprecipitation method. The LDH were then isolated after centrifugation, without further washing, and dispersed in a solution of ethanol and water containing PVP and PLL, which was then processed through centrifugal spinning. The resulting microfibers were then crosslinked using thermal treatment.

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Results: The intercalation of GA in the LDH structure was confirmed by XRD. Following the spinning process, smooth fibers with a dimensional range of 10-40 µm were obtained. The inclusion of LDH and the following thermal treatment did not affect the morphology and the dimensions of the microfibers. Furthermore, in vitro tests confirmed the cytocompatibility of the fibers on Normal Human Dermal Fibroblasts.

Conclusions: Centrifugal spun microfibers based on PVP and PLL doped with GA- LDH were produced. Future studies will be focused on the evaluation of the impact of the LDH on the polymeric structure, and the determination of the antioxidant and antibacterial properties of the microfibers due to the impact of gallic acid and polylysine, respectively.

Acknowledgements: CN thanks Programma Operativo Nazionale Ricerca e Innovazione (PON R&I 2014-2020, REACT-EU FSE DM 1061/2021) and SAES Getters SpA for his PhD position.

P100
ANTIBACTERIAL POLYMERIC NANOPARTICLES EMBEDDED INTO ZEIN SURFACE COATINGS AS A PROMISING TOOL FOR IMPROVING IMPLANT BIOACTIVITY

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Introduction: Bacterial adhesion, colonization, and biofilm formation onto the surfaces of implants can lead to high rate of rejection and failure of orthopaedic implants (1). For this purpose, the aim of this work was the design and development of antimicrobial NPs-doped films as bioactive coatings of orthopaedic implants.

Materials and Methods: PLA nanoparticles loaded with thymol were manufactured by the microfluidics method, using (ANP Automated nanoparticle system). Several processes parameters (total flow rate and ratios) were tested and their impact was evaluated (PDI, size). Subsequently, NPs were purified by dialysis and loaded into zein-based film by solvent casting techniques by dissolving zein (20% w/v) in hydroalcoholic solution (80%) and using different concentrations of glycerol as plasticizer. The zein based film doped with PLA-loaded thymol NPs was characterized using a multidisciplinary approach including morphology, particle size, zeta potential and mechanical properties and cytotoxicity towards NHDF cell line.

Results: Mechanical properties of undoped films with different concentrations of glycerol suggest that the 3% (w/v) of glycerol was the best concentration of plasticizer able to increase system elasticity. In additions, pre-formulative studies on NPs production show that the processes parameters variation had a significant impact on the particles size and smaller particles were obtained increasing the ratio aqueous/organic phase. In particular, the ratio 8:1 was the better ratio with a dimension around 194 nm +/- 4 nm and narrow size distribution (PDI<0.2). NPs were loaded into the film and the in vitro characterization suggested that the final systems were biocompatible towards fibroblasts cell and promoting cell proliferation.

Conclusions: Zein based films loaded with PLA-thymol NPs were successfully developed as coating materials for implants. Further studies are ongoing to assess the antimicrobial and biological properties.

Acknowledgements: This work was funded by project PNRR ON FOODS - PE0000003 - F13C22001210007.

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P101
INORGANIC NANOPARTICLES-DOPED NANOFIBROUS SCAFFOLD FOR SKIN REGENERATION

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Introduction: Natural polymers are considered promising biomaterials in regenerative medicine since they can provide a suitable microenvironment for wound healing, mimicking the structural and biochemical cues of native tissues. Scaffolds produced by animal proteins, such as gelatin, could sustain cell adhesion and proliferation due to the presence of tripeptide Arg-Gly-Asp (RGD) motifs, while scaffolds based on plant-based proteins, such as zein, have less immunogenic response than animal-derived proteins.

In addition, inorganic nanoparticles, such as selenium nanoparticles (SeNPs), can improve the wound healing process, thank to their antimicrobial activity against *Pseudomonas aeruginosa*, a pathogen involved in life-threating wound infections (2). In light of these considerations, gelatin or gliadin-based nanofibers doped SeNPs were designed and developed.

Materials and Methods: The polymeric blends were based on pullulan, an electrospinnable polymer, and proteins, gliadin or gelatine. Citric acid was added as crosslinking agent and SeNPs as antimicrobials. Nanofibrous scaffolds were obtained using horizontal electrospinning apparatus keeping the same variables for each formulation. the systems were made insoluble by heating, and imaged using electron microscopy (SEM and TEM). Physico-chemical properties, including the mechanical ones, were also assessed.

Results: SEM images revealed smooth surface and uniform nano-dimension fibers independently of scaffold compositions. In addition, after crosslinking and subsequent hydration, each scaffold retained a nanofibrous structure. TEM images confirmed fiber doping with SeNPs. Moreover, the mechanical analysis showed that the presence SeNPs led to increased elastic properties and Young modulus in the case of gelatine-basednanofibers.

Conclusions: Nanofibers based on proteins, doped with SeNPs, have been successfully developed. Current studies are ongoing to evaluate the effect of SeNPs on the preclinical properties of the fibers, in particular biocompatibility and antioxidant properties in vitro on fibroblasts.

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P102
PREPARATION AND IN VITRO EVALUATION OF POLYMERIC NANOPARTICLE FORMULATIONS CONTAINING CARVEDILOL

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Introduction: The aim of this study was to prepare an orally applicable polymeric nanoparticle (NP) delivery system containing carvedilol (CAR), which is a non-selective betablocker indicated after heart failure and myocardial infarction (1). Polymeric nanoparticles can be developed to target the drug to a specific area (2). In vitro dissolution tests were performed to evaluate release properties and improve the efficacy of the novel drug delivery platform.

Materials and Methods: CAR (gifted by DEVA Holding, Turkey), Eudragit S100 (Evonik, Germany). All other chemicals were in analytical grade. Ultraviolet (UV) Spectrophotometric method was used for the determination of CAR in validation experiments and pharmaceutical formulations (2). Carvedilol was analyzed at 242 nm wavelength. Eudragit S100 was used as the polymer in all formulations. CAR-loaded-NPs were prepared using Nano Spray-Dryer and nanoprecipitation method. 2 different formulations were prepared for the nanoprecipitation method; mono-emulsion and double emulsion. Properties of NPs were evaluated by particle size (PS), zeta potential (ZP), SEM, encapsulation efficiency (EE%), dissolution, release kinetics, NMR, DSC and FT-IR (3).

Results: CAR containing nanoparticle formulations were successfully prepared using Eudragit S 100. Formulations were characterized to evaluate their properties.

Conclusions: CAR containing polymeric nanoparticle formulations were developed to provide solutions to overcome problems of treatment with carvedilol. In the studies, the UV-spectroscopy method validated for carvedilol showed to be a selective and accurate method for quantification. Physicochemical structure and release properties were explained by various analyses. It was concluded that the developed formulations are a hopeful transporter for oral carvedilol delivery.

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P103
PREPARATION AND IN VITRO EVALUATION OF NORFLOXACIN-LOADED PLGA NANOPARTICLES FOR OCULAR APPLICATION

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Introduction: Norfloxacin (NFX), the broad-spectrum antimicrobial-acting analog of nalidixic acid, is a fluoroquinolone that has strong activity against gram-positive and gram-negative bacteria while having limited activity against anaerobes (1). Nanoparticles can deliver ocular drugs to specific target sites and hold promise to revolutionize the therapy of many eye diseases (2). Therefore the aim of this study was to formulate polylactic-co-glycolic acid (PLGA) nanoparticles for enhanced treatment of ocular fungal infections with the help of extended releases from polymeric nanoparticles.

Materials and Methods: NFX (Sigma, Germany), PLGA (Sigma, Germany). All other chemicals were in analytical grade. Nanoparticles were prepared by nanoprecipitation method [3]. A modified HPLC method was used for the determination of NFX [4]. Particle size (PS), polydispersity index (PDI) and zeta potential (ZP) analyses (Malvern Zetasizer, UK), FT-IR (IR Prestige-21 Shimadzu, Tokyo, Japan), DSC (Shimadzu DSC-60, Japan) and 1H-NMR (Ultra-Shield™ CPMAS NMR, Brucker, Rheinstetten, Germany) analyses, in vitro release studies and anticandidal activity studies were performed.

Results: Many formulations were prepared and compositions of the selected formulation with PS, PDI, ZP, NFX amounts (EE%) were presented in Table 1. FT-IR, 1H-NMR and in vitro release analysis results were presented in Figure 1-Figure 3 respectively. Anticandidal activity of the formulations were presented in Table 2.

Table 1. Composition and PS, PDI, ZP, analyses results of the selected formulation (Mean ± SE, n=3)

Code	NFX (mg)	PLGA (mg)	ACT (mL)	PVA 2% (mL)	PS (nm)	PDI	ZP (mV)	EE (%)
NP1	5	100	5	20	174.0±10.7	0.1±0.1	-5.8±3.7	18.6±0.0

NFX: Norfloxacin, PLGA: Polylactic-co-glycolic acid, ACT: Aceton, PVA: Polyvinyl Alcohol, PS: Particle size, PDI: polydispersity index, ZP: zeta potential, EE: Encapsulation efficiency

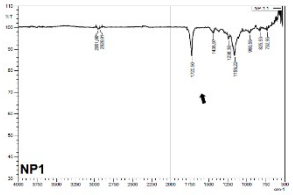

Fig.1. FT-IR

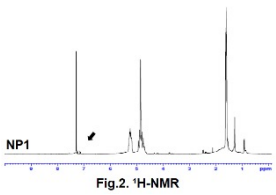

Fig.2. ^{1}H-NMR

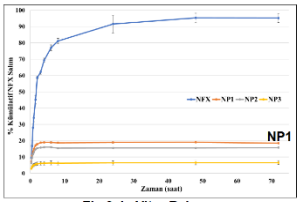

Fig.3. In Vitro Release
(Mean ± SE, n=3)

Table 2. Anticandidal activity of the formulations

MIC Values (µg/mL)					IC_{50} (µg/mL)
Code	***C. albicans***	***C. glabrata***	***C.krusei***	***C.parapsilosis***	**BJ Cell Line**
NFX	200	200	200	200	>500
PLGA	800	800	800	800	>500
NP1	25	50	100	100	305.55

Conclusions: PLGA based nanoparticles were formulated successfully for the topical application of NFX for enhanced treatment of severe ocular fungal infections.

Acknowledgements: To DOPNA-LAB for FT-IR and **1H-NMR analyses.** Anadolu University Scientific Research Project Foundation (Project Number: 2108S147) for financial support.

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P104
CYTOKINE GENETIC VARIANTS LINKED TO THE DEVELOPMENT AND COMPLICATION OF TYPE 2 DIABETES AMONG A GROUP OF TURKISH PEOPLE

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Introduction: Type 2 Diabetes is a metabolic abnormality characterized by a significant increase in blood glucose levels caused by a combination of environmental and hereditary causes, as well as micro and macrovascular problems. Researchers discovered correlations between disease and inflammation. Cytokines play an important role in homeostatic processes like tissue healing and inflammation. Single nucleotide polymorphisms (SNPs) in numerous cytokine genes affect their expression levels, increasing the risk of illness development. Finally, studies found strong connections among cytokine gene polymorphisms and the onset and advancement of type 2 diabetes. This study examined the relationship between IL-1β, TNF-α and IL-6 cytokine gene polymorphisms with Type 2 diabetes development and comorbidities in Turkish people.

Materials and Methods: All participants' DNA specimens were extracted, and the PCR-RFLP (Polymerase chain reaction-restriction fragment length polymorphism) technique was used for genotyping analysis.

Results: Our data indicate that TNF-α (-308) and IL-1β (+3953) gene polymorphisms have a substantial impact on disease progression (3.27 and 2.15, respectively) and complications (4.15 and 2.81).

Conclusions: Our findings imply that TNF-α and IL-1β gene polymorphisms play a significant impact in the development and progression of Type II diabetes in the Turkish population. Our research will add to the literature by exposing the influence of potential individual differences across races on the development of Type 2 diabetes.

P105
ASSESSMENT OF THE IMPACT OF POTASSIUM CYANIDE EXPOSURE AND THYROID HOMEOSTASIS ON JEWELRY WORKERS

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Introduction: In industry and production, cyanide and its salts are widely used. A number of neuropathic and thyrotoxic disorders in humans have been linked to long-term exposure to low amounts of cyanide, according to studies. Cyanide is quickly converted to thiocyanate, which is easily detected in bodily fluids and is a strong inhibitor of iodide transport by the metabolic pathways already in place. Workers in the jewelry industry may be exposed to potassium cyanide due to its use in the industry. Studies assessing the connection between thyroid homeostasis and cyanide exposure in workers are lacking. According to our literature research, it has been observed that no study has been conducted on this subject in our country. The purpose of this study was to investigate the potential effects of potassium cyanide exposure on thyroid hormone parameters (T3, T4, and TSH) in jewelry workshop workers, as well as changes in blood parameters, liver function, and kidney function, and to correlate these effects with exposure duration.

Materials and Methods: The working group (n=51) consisted of healthy male workers who had been working in a jewelry workshop for more than two years. Thiocyanate levels in urine samples taken from workers, T3, T4, TSH levels in blood samples, liver (alanine aminotransferase-ALT, aspartate aminotransferase-AST), and kidney (creatinine, glomerular filtration rate-GFR) function parameters and blood parameters were measured.

Results: It was determined that urinary thiocyanate levels increased significantly in all study groups compared to the control group (n=40). A significant correlation between urinary thiocyanate levels and TSH levels was evaluated as an indicator of the undesirable effect of cyanide exposure on thyroid hormones. While no significant change indicative of deterioration in liver functions was observed, a statistically significant decrease in GFR was found which was observed due to the increase in working time.

Conclusions: The findings show that manufacturing workers working in the jewelry industry are exposed to low doses of potassium cyanide and that exposure may alter kidney and thyroid function.

Acknowledgements: This study was conducted with the approval of "Lokman Hekim University Non-Invasive Clinical Research Ethics Committee" dated 10.10.2012 and numbered B.10.4.İSM.4.06.68.49.

P106
INVESTIGATION OF THE DNA DAMAGE-INDUCING PROPERTIES OF BPA, BPS, AND BPZ ON MCF-7 CELL LINE

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Introduction: Bisphenols, commonly used in the production of plastics, possess significant endocrine-disrupting properties, interfering with hormonal systems in organisms. Additionally, studies indicate their genotoxic properties, raising concerns about potential DNA damage. Due to these hazards, regulatory measures have been implemented, notably the ban on Bisphenol A (BPA) in various consumer products due to its adverse health effects. However, the introduction of bisphenol derivatives, such as Bisphenol S (BPS) and Bisphenol Z (BPZ), although marketed as safer alternatives, exhibit similar toxic effects. BPA is found in food and beverage containers, thermal paper, and dental sealants. Its substitutes, BPS and BPZ, are also utilized in similar applications, including thermal receipts, food packaging, and epoxy resins. Yet, these replacements may not significantly enhance safety over BPA, thus maintaining the risk of adverse health effects. Understanding the endocrine-disrupting and genotoxic properties of bisphenols is crucial for informed decision-making regarding their usage and regulation. For this purpose, we investigated the DNA damage-inducing properties of BPA, BPS, and BPZ on MCF-7 cell line by using COMET assay.

Materials and Methods: To examine DNA damage, MCF-7 cell line (Given MCF7's estrogen-positive nature, it's ideal for studying bisphenols targeting the reproductive system) was exposed to BPA, BPS, and BPZ at 0.1, 0.5, 1, 5, 10, and 50 µM concentrations and COMET assay was performed. H2O2 at 50 µM concentration was used as a positive control. Results are expressed as % tail intensity.

Results: All studied concentrations of BPA, BPS, and BPZ significantly induced DNA damage compared to control ($p<0.05$). BPS at concentrations of 5, 10, and 50 µM and BPZ at 50 µM concentration significantly induced DNA damage more than BPA.

Conclusions: According to our results, BPS and BPZ show DNA damage-inducing properties like BPA and are even more genotoxic than BPA at high concentrations. Further studies are imperative to comprehensively understand the genotoxic effects of bisphenols.

Acknowledgements: This study was supported by a grant of Ankara University Scientific Research Projects Coordination Unit (TDK-2022-2702).

P107
INVESTIGATING THE AMELIORATIVE EFFECT OF SITAGLIPTIN AGAINST TERT-BUTYL HYDROPEROXIDE INDUCED TOXICITY IN HEPG2 CELLS

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Introduction: As a multifunctional organ, the liver is highly vulnerable to drug-induced liver injury (DILI) due to its high metabolic rate and biotransformation capacity, which make it susceptible to both metabolism-related and drug-induced damage (1). One of the causes of hepatotoxicity is oxidative stress, which occurs when radicals formed during metabolism overwhelm the antioxidant defense capacity (2). The objective of this study was to examine the ameliorative effects of sitagliptin, which is endowed with anti-inflammatory, antioxidant, and anti-apoptotic properties, against damage induced by tert-Butyl hydroperoxide (TBHP) in HepG2 cells.

Materials and Methods: HepG2 human hepatocellular liver carcinoma cells were acquired from the ATCC (HB-8065™). The cell viabilities were determined using MTT and neutral red uptake (NRU) assays (3). The experiments were conducted by seeding 1x104 cells per well in 96-well microplates. Sitagliptin and TBHP at eight concentrations (1, 5, 10, 50, 100, 250, 500, and 1000 µM) were applied for 24 hours. Based on the obtained results, one concentration of TBHP that significantly altered cell viability and three concentrations of sitagliptin that did not significantly affect cell viability were selected. The selected concentrations of sitagliptin and TBHP were administered together, and their effects on cell viability were compared to the application of TBHP alone.

Results: According to the results of MTT and NRU assays, sitagliptin reduced cell viability at maximum levels of 20-25% in the tested concentrations. To assess sitagliptin's protective potential, concentrations of 10, 15, 50, and 100 µM were chosen, as these concentrations exhibited no cytotoxic effects. TBHP, on the other hand, inhibited cell viability at levels of approximately 80% in the highest three concentrations. The concentration of TBHP chosen was 250 µM. In combined exposure, no effect of sitagliptin on TBHP-induced cell inhibition was observed.

Conclusions: At the selected concentrations, sitagliptin did not alter the levels of TBHP-induced cell viability inhibition. Further investigation into sitagliptin's potential anti-inflammatory, antioxidant, and anti-apoptotic properties could be conducted by exploring different concentrations and/or endpoints.

Acknowledgements: This research did not receive any specific grant from funding agencies.

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P108
MICROPLASTICS AND THE EMERGING CONCERNS ABOUT FOOD SAFETY: A BIBLIOMETRIC PERSPECTIVE

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Introduction: Microplastics (MPs) are plastic particles with sizes less than 5 mm. MP pollution has recently become an emerging concern for human health after detecting MPs in various foods and drinking water. Studies detecting these particles in human biological samples, such as sputum and blood, have drawn more attention to the subject (1,2,3). Bibliometric methods are widely used to track the trends and impact of publications in specific research areas. Therefore, we aim to conduct a pilot bibliometric analysis of the literature focusing on MPs and food safety.

Materials and Methods: Bibliometrics is a useful method that analyzes the influence or value of studies and visually demonstrates research development in a chosen field through maps (4). To conduct the analysis, the WoS database was chosen for data collection, and the bibliometrix R-package and the VOSviewer were used as bibliometric tools to evaluate the retrieved publications statistically. In the scope of our topic, due to a basic inclusion criterion, 220 publications were retrieved and data were processed with the tools mentioned above.

Results: The annual scientific production on the topic seems to have increased from 1 article in 2014 to 72 articles in 2023. The most productive countries that publish articles on the topic seem to be China, India, and Portugal, followed by others. The most relevant authors in the field are Wang X, Guilhermino L, and Wang J, and the most relevant sources among the retrieved publications are Science of Total Environment, Chemosphere, and Environmental Pollution. When the word cloud and co-occurrence map of author keywords were considered, it was seen that microplastics, food safety, nanoplastics, food, and fish are mainly selected keywords in these articles, followed by many others such as seafood, food packaging, food chain, and risk assessment.

Conclusions: The topic is getting worldwide attention; many countries have contributed, and China is leading the way in publishing. Accordingly, seafood is getting more attention in the field. Among plastic polymer types, polystyrene has appeared in various articles. In conclusion, there is a growing body of literature on MPs and their effects on food safety. There is a need for more studies that expand the type of food sources in their research and focus on assessing the potential health risks.

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P109

DNA REPAIR CAPACITY IN RESPONSE TO HYDROGEN PEROXIDE-INDUCED OXIDATIVE DNA DAMAGE IN 3T3 CELL LINE

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Introduction: Oxidative damage in DNA, if it is not repaired, gives rise to significant biological phenomena including carcinogenesis, mutagenesis, and aging as well (1). Hydrogen peroxide (H2O2) is one of the main reactive oxygen species (ROS), leading to oxidative DNA damage by forming hydroxyl-free radicals by traversing the cell membrane using aquaporins (2). DNA damage induced by oxidative stress can be detected by using the comet assay, which is sensitive, quick, relatively straightforward, and cost-effective. The comet assay can be also used to investigate DNA repair (3). In our study, we aimed to examine DNA repair capacity as a time interval, which is the most popular DNA repair approach, in response to oxidative DNA damage induced by H2O2 in the 3T3 cell line.

Materials and Methods: The alkaline comet assay approach to measure DNA repair was used in this study. In our previous study, we determined the concentration and duration at which H2O2 caused maximum DNA damage as 50 µM for 30 minutes. Following this exposure, we changed the medium containing H2O2 to the fresh medium. For DNA repair, we selected the specific time intervals as 15, 30, 45 min, 1 hour, 2, 4, 6, 8, 16, and 24 hours. Each time interval was studied in duplicate. To assess the comet test outcomes, a total of 100 cells were examined for each sample using a microscope, and the corresponding data on DNA tail density were analyzed. Statistical analyses were performed employing the Repeated Measures Analysis of Variance (ANOVA) test through the SPSS software (Version 23.0 for Windows). The limit of statistical significance was taken as $p<0.05$.

Results: According to the results, it was observed that DNA damage during each designated time interval for DNA repair exhibited a statistically significant reduction compared to the DNA damage induced by exposure to 50 µM H2O2 for 30 minutes. Notably, DNA repair processes commenced at each time interval, and statistically approached the control group from the 6th hour.

Conclusions: Our results could provide valuable insights for future investigations, such as human biomonitoring studies, aimed at evaluating intra- and inter-individual variations in DNA repair capacity.

Acknowledgements: This study was supported by a grant of Ankara University Scientific Research Projects Coordination Unit (TYL-2022-2356).

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P110
THE SURVIVAL RATE OF ISOLATED LYMPHOCYTES UNDER DIFFERENT STORAGE CONDITIONS

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Introduction: Epidemiological and in vitro investigations play pivotal roles in the comprehensive evaluation of the toxicity associated with chronic diseases such as cancer. Among the biological samples, human blood is widely used. Lymphocytes isolated from blood emerge as a preferred choice, especially in DNA-related studies. The process involving the isolation, freezing, and storage conditions of lymphocytes can have a negative impact on the integrity of lymphocytic DNA (1,2). Consequently, in human biomonitoring studies, it is important to consider these effects to ensure the reliability and accuracy of the results. We aimed to contribute to DNA-related studies in which isolated lymphocytes are used by evaluating the survival rate of lymphocytes under various times and storage conditions.

Materials and Methods: A heparinized blood sample of 5 mL was obtained from a healthy volunteer. Lymphocytes were isolated using the leucosep tubes (12 mL, Greiner bio-one).

Following isolation, lymphocytes were subjected to storage at varying temperatures (-20°C and -80°C) for durations of 1, 3, 6, and 12 months. Additionally, a portion of lymphocytes stored under different temperature conditions for each time interval was preserved in a cryopreservative solution (10% DMSO), while another portion was stored directly. Following each designated duration, a volume of 20 µL of lymphocytes was added to an equal volume of trypan blue solution to ascertain cellular viability. The survival rate of lymphocytes was conducted utilizing a "TC20 Automated Cell Counter".

Results: Based on our findings, the survival rate of lymphocytes was found higher under -80°C storing conditions than at -20°C. Additionally, it can be stated that storing lymphocytes with a cryopreservative solution (10% DMSO) at -80°C provides a more optimal strategy for maintaining lymphocyte integrity.

Conclusions: Our results may provide foundational insights for researchers using lymphocytes in DNA-related investigations.

Acknowledgements: Seniha Kerimoglu's doctoral thesis from the Health Sciences Institute at Ankara University served as the basis for this work. With a grant number TDK-2022-2701, the Ankara University Scientific Research Projects Coordination Unit provided funding, which the authors gratefully recognize.

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P111
COMPARATIVE HEAVY METAL ANALYSIS OF TAR PHASES ISOLATED FROM THE MAINSTREAM SMOKES OF CONVENTIONAL CIGARETTES AND HEATED TOBACCO PRODUCTS

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Introduction: Smoking is one of the most important preventable causes of death and, in Turkiye, represents a major socioeconomic burden due to its relationship with the development and progression of chronic lung diseases. In addition, tar accumulated in cigarette butt filters can be discarded in urban areas, passing through storm sewers to streams and finally to the ocean, thus constituting an emerging environmental health concern (1). This study aimed to comparatively analyze the accumulated heavy metal profiles of manually isolated tar phases from a conventional cigarette (TarC) and from heated tobacco products (HTPs) (TarH).

Materials and Methods: TarC and TarH were isolated according to a slight modification of our previous method (2). Tar collected from each tobacco product (TP) on Whatman filter papers was digested with ultrapure HNO3 (67-69%) + H2O2 (30%) for 2 h at 80 ºC and analyzed via ICP-MS after diluting the sample solutions (1:10) with a diluent containing 2% HNO3, 500 µg/L Au and 10 µg/L internal standard (6Li, Sc, Ga, Y, In, Rh, Ir, Bi). Sample blanks were prepared with original paper filters. The content of the analyzed elements (7Li, 65Cu, 66Zn, 75As, 85Rb, 111Cd, 202Hg, 205Tl, 208Pb) were expressed as µg/g tar.

Results: Our findings indicated a significant difference in the heavy metal content of two different TP. The TarH samples had a lower heavy metal content, with values below the detection limit, while TarC samples contained detectable levels of Cd, Tl, Pb, Li, Zn and Rb. The most abundant metals were Zn (3.9 ± 0.4 µg/g) and Cd (3.5 ± 0.9 µg/g), respectively.

Conclusions: These results suggest that HTPs may represent a potential reduction in heavy metal exposure compared to conventional cigarettes. However, detailed research is necessary to elucidate the long-term health hazards of using HTPs and the potential presence of other harmful compounds in their tar. Future studies should explore the environmental impact of cigarette butt disposal, with particular interest in heavy metals leaching.

Keywords: Cigarette smoke, passive smoking, heated tobacco products, environmental pollution, heavy metal.

Acknowledgements: This project is supported by TUSEB 2023-A3-01 grant (#33176).

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P112
INVESTIGATION OF THE HEPATOTOXIC EFFECTS OF SOME HERBAL PRODUCTS BY IN VITRO METHOD

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Introduction: Ayurveda is a traditional medicine with a long history that dates back about 3,000 years, and it started in the Indian subcontinent. Complementary and alternative medicine is the unconscious usage of Atractylus gummifera and Senecio vulgaris, two Ayurvedic herbal preparations that belong to the Asteraceae family and vary according to the location in which they are utilized. The hepatotoxic effects and mechanisms of the Atractylis gummifera and Senecio vulgaris plants, which contain diterpene glycosides and pyrrolizidine alkaloids, respectively, and are widely used in Ayurveda, are not fully understood in humans.The aim of this study was investigate in vitro hepatotoxicity of the selected diterpene glycosides and selected pyrrolizidine alkaloids in the human hepatocellular carcinoma (HepG2) cell line, by MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide) assay.(1)

Materials and Methods: In this study, diterpene glycoside (atractyloside and stevioside) , pyrrolizidine alkaloids (senecionine and senecionine N-oxide) standards were tested at different concentrations. The MTT assay was performed to investigate the cytotoxic effects and evaluate the hepatotoxicity of different ayurvedic plants. All studies were conducted using HepG2 cell lines. This investigation was conducted using four distinct plant standards containing diterpene glycosides and pyrrolizidine alkaloids. These plant standards include atractyloside and stevioside (diterpene glycosides), as well as senecionine and senecionine N-oxide (pyrrolizidine alkaloids). The MTT test was used to explore the cytotoxic effects of these standards at various concentrations, as well as to assess the hepatotoxicity of our plant standards and other ayurvedic plants that included these plant standards. All experiments were carried out on HepG2 cell lines.

Results: According to the results obtained, three duplicate cytotoxicity studies utilizing MTT analysis, one of the colorimetric techniques, were carried out on HEPG2 (liver cancer cells) with five different dosages of four different plants. Senecionine N-oxide was shown to have a greater degree of toxicity than the other compounds, averaging 77.19% at 1600 qM. Furthermore, the lowest level of toxicity was demonstrated by 61.21% attained at an 800 qM dosage of senicionine.

Conclusion: Our investigation found that atractyloside, stevioside (diterpene glycoside), senecionine and senecionine N-oxide (both pyrrolizidine alkaloids) were cytotoxic to HepG2 cell lines. In the risk assessment of xenobiotics, it is critical to understand the toxicity pathways in order to predict potential risks.

Acknowledgements : This study was supported by a grant of BAP (TDK-2023-2853)

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P113
EVALUATION OF THE HEPATOTOXICITY OF HYDROXYCHLOROQUINE SULFATE IN RATS

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Introduction: Hydroxychloroquine sulfate (HCQS), a chloroquine derivative, is widely used in the treatment of malaria and rheumatic diseases and has also been used as an effective treatment option for coronavirus disease 2019 (COVID-19) due to both its anti-inflammatory and antiviral effects (1, 2). We aimed to investigate whether HCQS causes oxidative stress and DNA damage in rat liver at human-equivalent dose ranges administered in the treatment of COVID-19.

Materials and Methods: Rats were divided into six groups of eight animals each and doses of HCQS in the solution formulation were administered via gastric lavage. Group 1 and Group 4 (control groups) were given only sterile water and sacrificed 3 and 6 weeks later, respectively. Group 2 and Group 5 (treatment groups) were received the HCQS 2x3 mg loading dose on the first day, followed by a 1x0.9 mg maintenance dose for four days, and sacrificed after 3 and 6 weeks later, respectively. Group 3 and Group 6 (treatment groups) were received the HCQS 2x1.5 mg loading dose on the first day, followed by a 1x0.45 mg maintenance dose for four days, and sacrificed after 3 and 6 weeks later, respectively. Oxidative stress parameters such as catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), and malondialdehyde (MDA) were measured and the DNA damage was determined by using alkaline Comet assay.

Results: Changes after 3 weeks: Compared to the control group, a significant decrease in SOD and GPx activities were observed in both treatment groups, while there was an increase in MDA levels. Changes after 6 weeks: Compared to the control group, a decrease in SOD, CAT, and GPx activities were observed in both treatment groups, while there was a significant increase in MDA levels in both treatment groups. We also observed that DNA damage increased significantly in all treatment groups compared to their control groups at the end of both 3 and 6 weeks.

Conclusions: According to the findings, it was concluded that HCQS induced oxidative stress and DNA damage in rat liver.

Acknowledgements: This study was financially supported by Kahramanmaraş Sütçü İmam University Faculty of Medicine Research Foundation (Project No: 2020\4-14 M).

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P114
INVESTIGATION OF CYTOTOXICITY OF 2,4-D AND GLYPHOSATE BASED HERBICIDE USING ONCORHYNCHUS MYKISS (RAINBOW TROUT) LIVER CELLS (RTL-W1)

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Introduction: Industrial and agricultural activities, which are the result of development and change, increase the chemical burden of the environment; because many and many types of chemicals are circulating in the environment. These chemicals or chemical mixtures can be a potential threat to the aquatic biota. Regulatory agencies recommend conducting fish toxicity tests But, these regulations for the protection of aquatic organisms mean that hundreds of chemicals are evaluated in vivo on numerous fishes. However, the 3R approach, which is a guide to the ethical use of animals in experiments, has gained more importance recently (1).

Materials and Methods: RTL-W1 cells were seeded in 96-well plates at an initial cell number of 5 ×104 cells/well in 100 µl culture media. Subsequently, RTL-W1 cells (rainbow trout liver – waterloo 1; were exposed to selected herbicides. After 24 h of exposure, treated cells were analysed for cytotoxic effects by two different assays. Alamar blue/CFDA-AM assay was performed for investigation noninvasive cell. Independent experiments and technical replications were considered in triplicate.

Results: The cytotoxic and lethal effects of the test chemicals are listed as Hektafermin® > 2,4-D > Roundup Star® > Glyphosate, according to in vitro test results.

Conclusion: According to our results Commercial herbicide mixtures have greater cytotoxic and lethal effects than analytical standard mixtures, individual herbicide formulations, and analytical standards. The results are important in terms of ecotoxicology and may be useful in environmental risk assessment studies.

Acknowledgements: This study was supported by Ankara University Scientific Research Fund (Project No: 21L0237009).

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P115
PREDICTING ENDOCRINE DISTRUPTING AND DEVELOPMENTAL EFFECTS OF SYNTHETIC CATHINONES VIA IN SILICO EVALUATION

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Introduction: Synthetic cathinones are a type of psychoactive substance that is chemically similar to cathinone, a naturally occurring stimulant found in the khat plant (1). Synthetic cathinones are artificially created in laboratories and are often referred to as "designer drugs" because they are synthesized to mimic the effects of controlled substances like amphetamines, cocaine, and ecstasy (2,3). They increase synaptic dopamine, noradrenaline, and serotonin levels through interaction with monoamine membrane transporters (4). Exposure to synthetic cathinone is necessary for several reasons: Health risks, addiction potential, poisoning and death, mental health issues, and socioeconomic impact (5). Substances that cause addiction often interfere with the hypothalamic-pituitary-endocrine axis, resulting in an endocrine-disrupting effect (6). The increasing number of new substances coming onto the market each year, the rise in their use among young people, and the lack of toxicity data make it difficult to identify which ones are of real concern. Here, we aimed to evaluate the endocrine and reproductive effects of some commonly encountered synthetic cathinones with in silico methods.

Materials and Methods: The endocrine-disrupting effects and developmental toxicity of synthetic cathinones were studied using in silico methods implemented in the following software: VEGA NRMEA (v.1.1.1) and VEGA QSAR (v.1.2.3) tools on the VEGA-HUB platform, Danish (Q)SAR Database, and US EPA TEST (v.5.2.1). Predictions were compared with available experimental data.

Results: Out of the thirty (30) substances were predicted to be developmental toxicants in the both VEGA developmental toxicity model (CAESAR) and EPA TEST developmental toxicity model. The Developmental/Reproductive Toxicity Library (PG) model predicted thirty-nine (39) substances as developmental toxicants with good reliability. IRFMN-CERAPP model evaluated twelve (12) substances as possibly having estrogen receptor (ER)-mediated activity. Ethylone, Eutylone, Methedrone, and 4-Methoxy-α-pyrrolidinopropiophenone were predicted developmental toxicants with an ER-mediated effect.

Conclusions: These initial findings suggest that some synthetic cathinones may have detrimental impacts on the endocrine and reproductive systems through interactions with receptors.

Acknowledgements: This study received no specific grant from any funding agency. The developers of QSAR tools are gratefully acknowledged.

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P116
A PRELIMINARY STUDY ON THE EFFECT OF CITRUS SPECIES ON HEPATIC CYP1A1 ACTIVITY

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Introduction: The simultaneous use of herbal products with medicines increases the risk of interactions. Citrus fruit juices are one of the most widely consumed herbal products worldwide. Cytochrome P450 (CYP450) enzymes, which are important for xenobiotic and drug metabolism, are found in organs like the liver. CYP1A1 is an important isozyme involved in the metabolism of many drugs, such as caffeine, theophylline, paracetamol, riociguat, granisetron, axitinib, erlotinib, and conivaptan. Previous studies have reported that the juices of some Citrus species mainly grapefruit, cause drug interactions through modulation of CYP450 enzymes (1, 2). Upon review of the literature, there are a limited number of studies evaluating the efficacy of Citrus species on CYP1A1-mediated metabolism. This study aimed to investigate the effects of Citrus fruit juices on CYP1A1 activity.

Materials and Methods: The effects of 5 mg/mL doses of Citrus fruit juices on CYP1A1 enzyme activities in rat hepatic microsomes were investigated using the 7-ethoxyresorufin O-deethylase (EROD) assay. EROD activity is measured by following the CYP1A1-mediated deethylation of the substrate 7-ethoxyresorufin to form the product resorufin, which can be monitored fluorometrically. While caffeine was employed as a standard, the control used in this protocol was dimethyl sulfoxide (DMSO) in which the synthesized compounds were dissolved.

Results: Citrus sinensis (L.) Osbeck, Citrus japonica Thunb., and Citrus australasica F.Muell. fruit juices were found to inhibit CYP1A1 activity by 50%, 50%, and 60%, respectively (caffeine: 56%).

Conclusions: In this study, some Citrus species were predicted to affect CYP1A1 activity. The simultaneous use of C. sinensis, C. japonica, and C. australasica fruit juices with drugs metabolized by the CYP 1A1 isozyme should be monitored carefully.

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P117
PHARMACEUTICAL INDUSTRY AND SUSTAINABLE DEVELOPMENT GOALS

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Introduction: The Sustainable Development Goals developed by the United Nations guide all stakeholders to tackle defined problems for the planet and humanity. The goals set until 2030 guide businesses operating in both the public and private sectors (1-3). Within the scope of this study, we aimed to examine the sustainability reports of pharmaceutical companies in our country and the SDGs they contain.

Materials and Methods: The sustainability reports published by the member companies of the Association of Research-Based Pharmaceutical Companies, Pharmaceutical Manufacturers Association of Türkiye, Turkish Pharmaceutical Industry Association were accessed from the companies' websites, and the SDG contained in the reports were determined through the data collection form. The statistical differences in companies' reports in terms of SDGs were determined using SPSS.

Results: Of 128 companies, 58 sustainability reports were accessed. Thirty of them included SDGs, and only three companies covered all SDGs.

Conclusions: Sustainability is of critical importance in health-related sectors, such as the pharmaceutical industry, where people are affected in many ways and environmental impacts are prioritized. Developing and implementing business strategies within the scope of sustainability principles has become necessary for public health. Raising the awareness of all stakeholders in the sector on this issue is critical to ensure the continuity of the activities carried out and to understand their impact.

Acknowledgments: This study was supported by a grant of TUBITAK (BIDEB-2209A).

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P118
AN EVALUATION OF THE PHARMACIST COOPERATIVES WEBSITES

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Introduction: Cooperatives that support members in collaboration in various ways are also found in the pharmacy field (1). They should have a high level of interaction with their stakeholders, and for this purpose, use their websites effectively with specific features and tools, such as Lighthouse. In this study, the websites of the Association of All Pharmacists Cooperatives (TEKB) and its members, as well as the websites of some foreign pharmacist cooperatives, were examined, and suggestions for improvement were presented.

Materials and Methods: The websites of the pharmacy cooperatives were examined in terms of 19 criteria (phone number, e-mail address, product sales, language option, etc.) under 4 main headings (communication, social media, aesthetics, other) and Lighthouse criteria. The presence of the 19 criteria on the websites was scored as 1 and their absence was scored as 0; the elements requiring more detailed scoring were detailed. Lighthouse criteria were analyzed using their own extensions. Mann-Whitney U test was used to determine whether there was a statistical difference between the websites.

Results: There was no statistically significant difference between TEKB and five member cooperatives and four foreign cooperatives found by searching "pharmacy cooperative" on Google in terms of Lighthouse criteria.

Conclusions: The evaluation of elements for effective website usage to ensure stakeholder interaction through the development of information communication technologies is important for pharmacy cooperatives. The websites of the TEKB members provide high-quality standard content according to their activities, which increases their corporate quality and makes them more accessible to users.

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P119
HEALTH IN DIGITAL MEDIA: AN EVALUATION OF HEALTH-RELATED PODCASTS

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Introduction: Podcasts, a digital media tool for accessing health-related information, have become a resource used by many people during the COVID-19 pandemic (1, 2). In this study, it's aimed to evaluate health-related podcast in podcast broadcasting environments and to reveal their characteristics in terms of various variables.

Materials and Methods: Among the podcasts on Spotify and Podtail, the first 50 podcasts accessed between November 1-2, 2023, with the keyword "health" were included in the study. These podcasts were analyzed in terms of variables such as content type, length, publisher, and purpose, among the criteria for podcast evaluation in the literature (3), and their descriptive characteristics were revealed.

Results: In total, only 60 of the podcast episodes analyzed featured health experts. While 31 of these podcast episodes were prepared institutionally, 11 were prepared by communities. The remaining content was individually produced.

Conclusions: Due to the easy access to information through the developing information and communication technologies, the number of accessible contents is increasing and problems related to the accuracy of information are arisen. In this context, only half of the content analyzed in health-related podcasts, which is an important source of information, is produced by experts. Since the accuracy of the information obtained has important effects on public health, it is extremely important for healthcare professionals to take part in content production and to develop themselves in a way that they can produce reliable and attractive content.

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P120
AN EVALUATION OF PHARMACY EDUCATION IN TERMS OF PLANETARY HEALTH

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Introduction: Planetary health concerns the health of humanity and the natural systems on which it depends and requires the inclusion of the issue of planetary health in the educational curriculum of healthcare professionals (1-3). In this study, it is aimed to evaluate the pharmacy education in terms of the Planetary Health Report Card (PHRC).

Materials and Methods: The Planetary Health Report Card, as a guide for students' evaluation, consists of five main headings: curriculum, planetary health research, community outreach and advocacy, support for student-led initiatives, and campus sustainability. In this study, pharmacy faculty students evaluated their education on these topics.

Results: The Faculty of Pharmacy was graded as D, B-, F-, D and C in five main headings according to the evaluation based on educational content and student experiences. The overall rating was D+.

Conclusions: As a result of the first evaluation conducted in Turkey within the scope of the PHRC, which evaluated only six pharmacy faculties worldwide, it was thought that student awareness could be increased with courses on climate crises, environmental toxins, carbon footprints, and their effects on health. The dissemination of PHR, a concept that should be taken into account in curriculum updates, as FIP emphasized, is essential for the training of pharmacists sensitive to planetary health.

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P121
PROMOTING ETHICAL LEADERSHIP IN COMMUNITY PHARMACIES

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Introduction: The field of ethics has its roots in ancient Greek philosophy and has come to encompass an individual's ability to distinguish between right and wrong when making decisions. Ethical leadership has emerged as a response to the moral crises businesses face today, and it involves making decisions guided by ethical values (1). Pharmacists play a critical role in community pharmacies as leaders and responsible managers. Pharmacists must lead while considering ethical values to provide high-quality and dependable services to society. Pharmacists can contribute to a healthier society by providing quality service to individuals. This study aims to uncover the attitudes of community pharmacy managers towards their staff and patients based on their knowledge and experience of ethical leadership (2).

Materials and Methods: The data for the study was collected through a survey specifically designed for community pharmacy managers in Turkey. This survey was distributed by sharing Google Forms links exclusively within social media groups for community pharmacists and on pharmacy chamber web pages. The survey consisted of questions using a 5-point Likert scale, and 97 participants voluntarily participated in the survey.

To analyze the data, SPSS ver. 25.0 was used, and it was determined that the data met the normality assumption. Parametric tests, such as independent groups t-test and ANOVA tests, were performed to analyze the data.

Results: The Cronbach's Alpha value of the measurement tool was found to be 0.703. The study reveals that there are notable variations in ethical leadership ($p<.05$) among different groups. Specifically, pharmacists employed in local pharmacies outperformed those working in healthcare institutions such as hospitals and Family Health Centers. Similarly, single pharmacists demonstrated better ethical leadership skills than their married counterparts. Additionally, pharmacists who received prior training in ethical leadership scored higher on the measurement tool compared to those who didn't undergo such training.

Conclusions: The study's findings suggest that the volunteers are proficient in essential areas such as ethics, professional ethics, and transparency with patients, as evidenced by their high participation rates. Ethical considerations were particularly important to the participants. However, not all participants showed the same level of engagement in statements related to organizational justice and employee relationships. The study also emphasized the necessity of further leadership training for pharmacists.

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P122
COMMUNITY PHARMACISTS AS KEY PLAYERS IN HANDLING NEGATIVE OUTCOMES

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Introduction: Community pharmacies in Turkey serve as the primary point of contact for patients seeking healthcare services. As healthcare professionals, pharmacists play a crucial role in ensuring effective drug treatments and safeguarding the health of patients. Possessing extensive knowledge of drugs and drug treatments, pharmacists provide the appropriate medication in the correct dosage and form to prevent adverse drug reactions and interactions (1).

Community pharmacists are responsible for a multitude of tasks, including financial obligations, pharmacy accounting, and inventory management. However, as both a healthcare institution and a business, pharmacies may be exposed to negative effects such as violence, stress, mobbing, and work accidents (2).

This study aims to investigate the responsibilities of pharmacists in managing the difficulties encountered in community pharmacies and the potential negative impacts they may have.

Materials and Methods: The data for the study was collected through a survey specifically designed for community pharmacists in Turkey. This survey was distributed by sharing Google Forms links exclusively within social media groups for community pharmacists and on pharmacy chamber web pages. The survey consisted of questions using a 5-point Likert scale, and 96 participants voluntarily participated in the survey.

To analyze the data, SPSS ver. 25.0 was used, and it was determined that the data met the normality assumption. Parametric tests, such as independent groups t-test and ANOVA tests, were performed to analyze the data.

Results: The Cronbach's Alpha value of the measurement tool was found to be 0.879. According to the study results, the average scores of male pharmacists participating in the study on financial management and effective communication within the pharmacy are statistically significantly higher than female pharmacists ($p<.05$).

Conclusions: Community pharmacists can enhance their own well-being and improve the quality of services for patients and pharmacies by addressing negative factors.

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P123
DESIGNING A RESEARCH STUDY ON SIGNAL MANAGEMENT FOR QUALITY ASSURANCE WITHIN A MEDICINAL PRODUCTS REGULATORY SCIENCES SCENARIO

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Introduction: Effective signal management strategies within pharmaceutical regulation contributes to the enhancement of the regulatory quality management framework, thereby strengthening regulatory mechanisms to safeguard the availability of good quality, safe and effective medicinal products. The setting of this research is at the Malta Medicines Authority. The competent Authority for regulating medicines and medical devices. The major functions consist of Licensing, EU Good Manufacturing Practices Inspectorate, and Pharmacovigilance. The Authority contributes to pharmaceutical science regulation through other activities such as an accredited academy, control of cannabis for medicinal and research purposes and medicines intelligence and accessibility. The aim is to investigate disruptive phenomena within operational medicinal products regulatory sciences on the contribution of signal management.

Method: A retrospective analysis of internal audits, quality improvement forms and deviation forms is carried out at the Malta Medicines Authority.

1. Identification of components required to develop a systematic framework to examine signal assurance within the domain of regulatory sciences.
2. Developing signal assurance (detecting, interpreting and managing signals) keeping outcome of the raison d'etre of regulatory sciences (safety, quality and efficacy).
3. Addressing patient centric versus policing approach in a regulatory environment
4. Devising a scientifically oriented style.
5. Crafting educational aspects including terminology.

Results: The results identified the following research design are divided into five phases. Phase 1, identification of signals through a retrospective documentation analysis via examination of internal audit reports, quality improvement forms and deviation forms. Phase 2, categorisation and validation of signals through an assessment tool, classifying the description, characteristics and actions required of a signal into severe, critical, major, minor and other. Phase 3, establishment of a trend towards concordance as a regulatory parameter as an evolvement concept of compliance and adherence expectations. Phase 4, developing a signal optimisation action plan through the introduction of innovative concepts and procedures such as patient centric concept versus policing and self-inspection versus self-assessment. Phase 5, developing an education program including new terminology such as the concept of "signalomics".

Conclusion: This study delves into the research design for investigating the confluence of data, communication, and governance dynamics, specifically concentrating on optimising signal management through an educational medium. The establishment of educational resources to facilitate the comprehension of how organisations perceive, interpret, and response to signals is proposed. The concept of signal management in quality assurance can be applied to various contexts within the pharmaceutical scenario including pharmaceutical technology.

P124
PHARMACOPOEIA ANALYSIS OF SOME PLANT MATERIALS SOLD AS CALENDULA (CALENDULA OFFICINALIS L.) IN THE MARKET

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Introduction: Calendula officinalis L., known as "calendula" in Turkey, belongs to the Asteraceae family. It has been reported that Calendula officinalis exhibits various biological activities, including angiogenic, vascular regeneration, analgesic, antimicrobial, antioxidant, and immunomodulatory (1). The unconscious use of non-standardized herbal products may render the treatment ineffective rather than positive, leading to undesirable results. The fact that many herbal products in the market do not meet pharmacopoeia standards emphasizes the importance of the study. This study aimed to analyze the standardization and therapeutic effectiveness of herbal products available in the market.

Materials and Methods: One of the C. officinalis drug samples used in the study was obtained from the internet, and the others were obtained from herbalists from different districts of Ankara. In the study, Turkish Pharmacopoeia 2017 was used as the reference. The Samples were analyzed in accordance with the "Calendula flos" monograph, the section related to the flowers of the C. officinalis plant, which is the part used for medicinal purposes. All experiments specified for analysis in the pharmacopoeia were performed in 3 repetitions for seven separate samples, and according to the average results of the experiments, it was determined whether the samples were suitable according to the pharmacopoeia, or not (2).

Results: As a result of macroscopic examinations, it was observed that the plant parts examined contained parts of C. officinalis plants, however other materials were also found to be present. The samples conformed to the pharmacopeia regarding microscopic analysis, chromatographic analysis, loss on drying, and ash amount tests. As a result of the foreign substance test, at least two types of foreign substances that should not be present in the drug were found in each sample. The percentages of flavonoids found in the spectrophotometric analysis were calculated outside the pharmacopoeia standards for all samples.

Conclusions: When all specifications were examined in the light of the analysis, it was seen that none of the samples were in compliance with the Turkish Pharmacopoeia 2017.

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P125
INVESTIGATION OF CHEMICAL COMPOSITION AND ANTICANCER ACTIVITY OF STACHYS OFFICINALIS (L.) TREVISAN SUBSP. BALCANICA (P.W. BALL) R. BHATTACHARJEE ESSENTIAL OIL.

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Introduction: Cancer, poses a significant global health burden with millions of cases diagnosed annually. Amidst this challenge, the therapeutic potential of plant-derived essential oils, particularly those from the Stachys genus, garners attention for their diverse pharmacological activities, including anticancer properties (1,2). This study focuses on Stachys officinalis subsp. balcanica, aiming to elucidate its essential oil's chemical composition and evaluate its potential in cancer treatment (3).

Materials and Methods: S. officinalis subsp. balcanica specimens were determined as plant material. The essential oil was extracted via hydrodistillation following the European Pharmacopoeia guidelines. Thin Layer Chromatography, Gas Chromatography and Gas Chromatography-Mass Spectrometry were used for separation and identification of chemical components of the essential oil. Antiproliferative and cytotoxic activities were assessed using Caco-2 and Vero cell lines. MTT assays were conducted to evaluate cell viability following treatment with different concentrations of the essential oil.

Results: The phytochemical analysis of S. officinalis subsp. balcanica essential oil (SOBEO) revealed a diverse composition, with 32 compounds identified, constituting 82.7% of the essential oil. The most abundant compounds were α-selinene (12.1%), β-selinene (11.4%), and β-caryophyllene (7.2%). Antiproliferative assays conducted on Caco-2 colon cancer cells showed significant inhibition of cell growth (41.56%) at 48 hours post-treatment with 5 µg of SOBEO. Conversely, cytotoxicity assays on Vero normal cells demonstrated no significant adverse effects following exposure to SOBEO.

Conclusions: This study represents the first comprehensive exploration into the phytochemical composition and potential anticancer effects of S. officinalis subsp. balcanica. Through anticancer activity analyses, we assessed its potential as a natural therapeutic agent against cancer. Given the limited existing research on this subspecies, our investigation fills a crucial gap in understanding its chemical structure and biological properties.

Acknowledgements: This research was supported by a grant provided under the "TÜBİTAK–2209-B Industrial Oriented Undergraduate Research Projects Support Program."

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P126
PHARMACOPOEIAL ANALYSIS OF SOME PLANT MATERIALS SOLD IN THE MARKET AS FLAXSEED (LINUM USITATISSIMUM L.)

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Introduction: Linum usitatissimum is one of the oldest plants. It has high amounts of fat, protein, dietary fiber, lignans, vitamins and minerals. Flaxseed has antimicrobial, antifungal, anticancer and antioxidant, laxative effects. It is used in constipation, gastritis, enteritis, irritated colon syndrome, diverticulitis and painful skin inflammations. In this study, plant samples sold in the market under the name of "Flaxseed" were investigated for their compliance with the specifications in the Turkish Pharmacopoeia 2017 monographs in order to be used for therapeutic purposes. (1-2)

Materials and Methods: In this study, flax seeds obtained from herbalists in 4 different cities (Denizli, Ankara, Izmir, and Muğla) and 4 different markets were used as study materials. The 8 flaxseed samples were coded with the numbers 1, 2, 3, 4, 5, 6, 7, and 8. Macroscopic and microscopic analysis and loss on drying, foreign matter, total ash determination, cadmium analysis, swelling ındex test were performed on flaxseed samples according to Turkish Pharmacopoeia. In the swelling ındex and macroscopic analysis, the drugs were used whole and in the other tests, the drugs were grinded in a grinding mill. In microscopic examinations, the samples were examined and photographed at 10x and 40x magnification with Leica CME microscope using chloralhydrate and Sartur reagent.

Results: According to the results of macroscopic and microscopic analysis, loss on drying, total ash, foreign matter test, all seeds comply with the pharmacopoeial limits. According to the results of the swelling ındex test, only the 3rd sample complies with the pharmacopoeial limits. According to the results of cadmium analysis, samples 2, 6, 7 and 8 were found to comply with the pharmacopoeia.

Conclusions: In this study, 8 samples taken from plant samples sold in the market under the name "Flaxseed" were found to be the correct plant, but they did not meet all the specifications in the Turkish Pharmacopoeia 2017 monographs for therapeutic use. These results present a negative public health implication for people who want to use these samples for medical treatment.

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P127
INVESTIGATION OF ANTIBACTERIAL ACTIVITY OF TERTIARY ALKALOID RICH EXTRACT AND ZINC NANOPARTICLES SYNTHESIZED FROM MANDRAGORA OFFICINALIS L.

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Introduction: The resistance of bacteria to antibiotics is a global challenge1. Therefore, it is necessary to investigate the tertiary alkaloid extract and zinc nanoparticles synthesized from Mandragora officinalis L. against some bacterial strains.

Materials and Methods: The air-dried plant material was extracted by percolation using methanol at room temperature in a plant to solvent ratio of 1:5 respectively. The methanol extract was concentrated over a water bath at 65 oC and then dried in an air drying oven at 30 oC. The tertiary alkaloid was obtained by dissolving the dried extract in 5% HCl. The acidic extract was filtered under vacuum and then shaken with petroleum ether to remove fat soluble substances. The aqueous layer was made alkaline (PH:7-8) using 25% ammonia solution. The alkaline extract was fractionated with chloroform in a separating funnel and the chloroform portion was treated with anhydrous Na2SO4. The chloroform fraction was filtered under vacuum and evaporated to dryness to produce tertiary alkaloid extract. The zinc nanoparticles were synthesized using 5 mM ZnNO3 solution with the tertiary alkaloids in the ratio of 9:1 respectively. The nanoparticles were characterized using UV, IR, Zeta sizer and XRD. Minimum inhibitory concentration (MIC) was used to determine the antibacterial activity by microdilution method against clinical strains of Escherichia coli and Staphylococcus aureus. Zinc nanoparticle 5 mg/mL, tertiary alkaloid 10 mg/mL, unloded ZnNO3 5 mg/mL (negative control) DMSO 15 % (negative control) and amoxicillin 3.75 mg/mL was used as positive control.

Results: The tertiary alkaloid and the zinc nanoparticles inhibited the growth of *Escherichia coli* and *Staphylococcus aureus* with MIC of 1.25 mg/m Land 0.625 mg/mL respectively. The results are presented in Table 1.

Table 1: Minimum Inhibitory Concentration

MIC in mg/mL					
Bateria	**ZnNPs**	**TA**	**$ZnNO_3$**	**DMSO**	**AMX**
S. aureus	0.0625	1.25	0	0	0.117
E. coli	1.25	2.5	0	0	0.117

ZnNPs= Zinc nanoparticles; TA=Tertiary Alkaloids; ZnNO3=Zinc nitrate & AMX=Amoxicillin

Conclusions: The zinc nanoparticle produced from Mandragora officinalis was effective against Gram positive and negative bacteria.

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P128
CHEMICAL COMPOSITION OF SCROPHULARIA XANTHOGLOSSA BOISS. ESSENTIAL OIL

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Introduction: The Scrophularia L. genus (Scrophulariaceae) is characterized by 76 species in Turkey, 37 endemics. Scrophularia species have been used in traditional medicine to treat skin disorders, dermatitis, and cancer (1,2).

To our knowledge, the previously volatile composition of *S. xanthoglossa* was not identified. Therefore, in this study, the chemical composition of essential oil (EO) was investigated by GC-MS and GC-FID.

Materials and Methods: In this study, the aerial parts of *Scrophularia xanthoglossa* was collected in Dallıca- Elazığ, Turkey, in 2021. The plant material was identified by the Dr. U. Çakılcıoğlu (Herbarium number: UC-12-2). The essential oil (EO) of *S. xanthoglossa* aerial parts was obtained by hydrodistillation using a Clevenger type apparatus for 3h. Essential oil was analysed both by GC-FID and GC-MS, simultaneously.

Results: The major components of essential oil were hexadecanoic acid (55.2%), hexahydro farnesyl acetone (5.4%) and heptacosane (5.2%).

Conclusions: This study is the first research on the volatile compounds of S. xanthoglossa essential oil. Based on our results, the essential oil of Scrophularia umbrosa from China contains hexahydro farnesyl acetone as the major compound (3). These two types were closer than the other species regarding chemical composition.

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P129

ANTIMICROBIAL, ANTIBIOFILM, AND ANTI-QUORUM SENSING (ANTI-QS) ACTIVITIES OF SCUTELLARİA YİLDİRİMLİİ M. ÇİÇEK & A.E. YAPRAK

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Introduction: Scutellaria genus (Lamiaceae) is represented by nearly 500 species and is known as "skullcap" in the world. Scutellaria species have been used to treat many diseases, including hepatic and gastric disorders, respiratory, cardiovascular, neurological diseases, and cancer (1, 2). This study aims to evaluate the antimicrobial, antibiofilm, and anti-quorum sensing (anti-QS) activities of Scutellaria yildirimlii extracts.

Materials and Methods: The dried aerial parts of Scutellaria yildirimlii was extracted with the mixture of ethanol: water. Furthermore, petroleum ether (PE), ethyl acetate (EAE) and aqueous sub-extracts (AE) were obtained, respectively. The broth microdilution method was used for the determination of MIC (Minimum Inhibitory Concentration) values of the extracts. In the antibacterial activity tests, Staphylococcus aureus, methicillin-resistant S. aureus, Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae were used as test bacteria and Candida albicans was used as test fungus. Antibiofilm activity was tested against Pseudomonas aeruginosa using the crystal violet assay, and the reporter bacteria Chromobacterium violaceum was used in the quantitative anti-QS activity test. The qualitative anti-QS activity test was performed according to the MIC values of the plant extracts against Chromobacterium violaceum.

Results: Total extract (TE) and petroleum ether extracts showed the best antibacterial activity. Only the petroleum ether extract demonstrated antifungal activity against Candida albicans, with a MIC value of 625 µg/mL. The percentage biofilm inhibition values of plant extracts (AE, TE, PE, EAE) (2500 µg/mL) were determined to be 76.79%, 57.47%, 54.81%, and 51.09%, respectively. The MIC values of the extracts range from 625 to 10000 µg/mL.

Conclusions: This shows that extracts obtained from S. yildirimlii are promising in the drug development phase against increasingly widespread antibiotic-resistant bacteria. The potential of the plant should be evaluated further.

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P130
ESSENTIAL OIL COMPOSITION OF THE AERIAL PART OF ANKARA ENDEMIC PRANGOS DENTICULATA FISCH. ET MEY.

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Introduction: Prangos denticulata Fisch. et Mey. is an endemic plant with a limited distribution in Ankara, growing only on Hüseyin Gazi Hill. Although this genus has important aromatic species in Turkey, there are only a few studies related to the phytochemical activities in this plant (1). Thus, in this study, the chemical composition of the essential oils from the flowerless aerial part of P. denticulata was analyzed for the first time.

Materials and Methods: The aerial part of *P. denticulata* was collected from Hüseyin Gazi Hill in July 2023 and was dried on filter paper in a cool area out of direct sunlight. The plant material was crudely cut into pieces and essential oil was extracted by hydrodistillation method for 2 hours in Clevenger apparatus. Xylol was added to the apparatus during the distillation process due to the low amount of plant material. The essential oil content was analyzed by GC-FID/MS (Voucher specimen, Ankara University, no: AEF 30942).

Results: The yield of the essential oil in the aerial part was 0.3% (v/w). The major compounds of the oil were determined as *p*-cymene (44.87%), caryophyllene oxide (34.24%) and 3-octanol (5.81%).

Conclusions: The essential oil yield from the aerial part of *P. denticulata* was comparable with other species (below 1%). The major compounds, *p*-cymene and caryophyllene oxide, were considerably higher compared to other species (1). The *p*-cymene ratio was more than twice that in the fruits of *P. denticulata* (2). Accordingly, it is clear that the essential oil composition in each organ is quite different from each other and will have different results in terms of biological activity. Therefore, there is a need for further research on the plant.

Acknowledgements: This study was supported by a grant of TUBITAK (1919B012307853)

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P131
PHYTOCHEMICAL EVALUATION OF TOMATO PASTE FACTORY BY-PRODUCTS: "AYAŞ" AND "EGG TOMATO" SEED OILS

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Introduction: Solanum lycopersicum L. is an economically important crop, and Turkey was the third larger tomato producer in 2020 (1). In aromatherapy, tomato seed oils are used as a carrier base oil for essential oils. The oil is antioxidant due to its lycopene content and therefore has a long shelf life (2). One of the main disposal issues facing the industry in question is plant food processing by-products. In this study, we aimed to compare the fatty acid and sterol composition of "Ayaş tomato" seed oils, a registered Ankara specialty and "egg tomato" by-product seeds, a variety commonly used in tomato paste production.

Materials and Methods: Tomato seeds of both varieties produced as a by-product were supplied from Ayaş, Ankara. The seeds were subjected to Soxhlet extraction. The seed oils were analyzed for sterol composition and fatty acid composition by GC analyses carried out at TÜBİTAK.

Results: As a result of extraction, seed oil yields were 17.98% and 10.28% for "Ayaş" and "egg tomato", respectively. GC analyses of the oils revealed that, linoleic acid (51.71%), oleic acid (23.26%) and linolenic acid (1.70%) were major unsaturated fatty acids in Ayaş tomato seed oils. Similarly, the major unsaturated fatty acids in egg tomato seed oils were linoleic acid (49.44%), oleic acid (26.13%) and linolenic acid (1.61%). Sterol analysis revealed that β-sitosterol and delta5-avenasterol were the major sterols in both oils. The sterol content of Ayaş tomato seed oils (7545.18 mg/kg) was higher than that of egg tomato seed oil (6305.02 mg/kg).

Conclusions: The use of bioactive ingredients can increase the efficiency of tomato industry and possibly reduce the harm that tomato by-products cause to the environment. As a result, no significant differences were found in the fatty acid composition of the two different oils. However, the sterol content of Ayas tomato seed oil is found to be higher. This shows that Ayaş tomato seed oil is more suitable for skin use.

Acknowledgements: This study was supported by a grant of TUBITAK 2209 (1919B012218840).

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P133
STUDIES ON INSECTICIDAL EFFECT AND PHYTOCHEMICAL PROPERTIES OF CYANUS DEPRESSUS (M. BİEB.) SOJÁK

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Introduction: The Asteracea family is one of the largest families among all known families. It has annual or perennial species growing in a wide geography ranging from Central and Southern Europe, Asia and Northern Europe. Centaurea depressa, known synonymously as Cyanus depressus (M. Bieb.) Soják, is an annual plant with deciduous leaves in herbaceous form growing in Central Asia (1). Centaurea species have antimicrobial, anti-inflammatory, antiprotozoal and cytotoxic effects (2). Studies have shown that Centaurea species are rich in flavonoids, lignan glycosides and sesquiterpene lactones (3). In this study, insecticidal activity of different extracts of C. depressus was studied together with the characterization of some of the secondary metabolites

Materials and Methods: The plant was collected near Haymana road, Ankara. Extracts were obtained from the aerial parts using three different solvents (MeOH, EtOAc and n-hexane) and two different extraction methods (Soxhlet and ultrasonic extraction). For insecticidal activity studies, the extracts were applied topically on two different agricultural pests (Tribolium castaneum and Sitophylus oryzae). Mortality rates on these two species were observed in 24 h and 7 day periods. Qualitative analysis of the MeOH extracts was performed using TLC, HPLC and HPTLC techniques.

Results: As a result, it was observed that methanolic extracts prepared by Soxhlet and ultrasonic extraction methods showed higher insecticidal effect on both agricultural pests (T. castaneum and S. oryzae). When the extraction methods were compared, it was clear that the Soxhlet extraction method possesed a higher insecticidal effect. Chromatographic analysis revealed the presence of gallic acid, chlorogenic acid and luteolin in the extracts.

Conclusions: In the present study, the insectisidal activity of C. depressus on T. castaneum and S.oryzae was investigated for the first time.

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P134
EVALUATION OF CYTOTOXIC POTENTIAL OF ENDEMIC DIANTHUS GOEKAYI ON MCF-7 AND MDA-MB-231 CELL LINES

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Introduction: The genus Dianthus L. (Caryophyllaceae) is represented with more than 300 species, mainly distributed in the Mediterranean region of Europe and Asia. There are about 92 species of the Dianthus genus in Turkey, 49 of which are endemic (1). Dianthus goekayi Kaynak, Yılmaz & Daşkın is a perennial endemic plant that grows in Bursa and Kütahya provinces, Turkey (2). Dianthus species has a rich source of triterpenoid saponins, flavonoids, and essential oils, according to earlier chemical studies on the species. Pharmacological investigations demonstrated that Dianthus species had analgesic, antioxidant, cytotoxic and antimicrobial properties (3,4).

Materials and Methods: In the current study, the methanol extract and its petroleum ether, CHCl3, EtOAc, and n-BuOH fractions and water extracts of endemic Dianthus goekayi were investigated for their cytotoxic activity against MCF-7 and MDA-MB-231 cell lines by the MTT method after 24 h of treatment. For the positive control, the cells were treated with the chemotherapeutic drug cisplatin, which has been widely used in a range of cancers.

Results: According to the results, the CHCl3 fraction of the methanol extract is the most active sample, and it has moderate cytotoxic activity with 57.10±2.87 µg/mL and 131.2±3.121 µg/mL IC50 values on MCF-7 and MDA-MB-231 cell lines, respectively.

Conclusions: All the tested extracts and fractions showed cytotoxic activity on both cell lines in a dose-dependent manner. It is the first cytotoxic activity study of D. goekayi against MCF-7 and MDA-MB-231 cell lines.

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PHARMACOPEIAL ANALYSIS OF EUCALYPTUS ESSENTIAL OILS

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Introduction: The genus Eucalyptus, belonging to the Myrtaceae family, involves approximately 800 species in the world. Eucalyptus L'Hér. species are known for their essential oils that are composed of a variety of biologically active compounds, including terpenoid compounds, phenolics, and flavonoids (1). Essential oils extracted from Eucalyptus species, predominantly through distillation methods, are utilized in pharmaceuticals, perfumery, and industrial sectors (2). Rich in eucalyptol, citronellal, citral, or α-phellandrenes, these oils exhibit medicinal properties, including antibacterial, anti-inflammatory, antioxidant, and anti-tumor activities (3). Eucalyptus essential oils are frequently used in medical formulations offered by companies and are used regularly in our daily lives, even if we are not aware of it.

Materials and Methods: In this study, it was aimed to determine the compliance of the samples sold under the name of "Eucalyptus essential oil" in our country and abroad with the characteristics specified in the Turkish Pharmacopoeia 2017 monograph. For this purpose, samples were purchased from herbalists in Ankara and Egypt. In order to determine the compliance of the samples with the Turkish Pharmacopoeia 2017, their solubility in alcohols at various concentrations, whether they contain aldehydes, refraction cursor measurement, relative densities and chromatographic profiles using TLC method were determined.

Results: The results of each experiment for six different essential oils examined in total were transferred to tables, and only two of these six different essential oils in the final table created based on the results in these tables were suitable to the pharmacopoeia.

Conclusions: The negative test results of essential oils of foreign origin show that the abuse of essential oils, which can be sold at extremely high prices compared to those in our country and can be used among the public with their pharmacological effects, cannot be ignored.

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P136
MORPHOLOGICAL AND ANATOMICAL STUDIES ON HERBAL MATERIALS SOLD IN THE MARKET AS MALLOW (MALVA SYLVESTRIS L.)

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Introduction: Malva sylvestris L. (Mallow) has long been used in traditional medicine. It contains high levels of mucilage, phenolic compounds, coumarins, proteins and polysaccharides. Scientific studies have proven the anti-inflammatory, antimicrobial, antioxidant, hepatoprotective, antitussive and laxative effects of mallow. In our country, medicinal plants are sold in the market. It is important that these plants are collected correctly, identified correctly and sold by people who have knowledge of their uses. The mallow flower and leaf drugs used in this study were obtained from herbalists from different parts of Ankara. Morphological and anatomical studies were carried out according to the monograph in the Turkish Pharmacopoeia 2017. Its suitability according to the Turkish Pharmacopoeia 2017 was evaluated (1).

Materials and Methods: A total of 10 samples sold under the name of mallow were taken from herbalists from different districts of Ankara. For microscopic examination, preparations were prepared using chloral hydrate reagent and examined under a Leica CME microscope and photographed at 10x and 40x magnification with a camera attached to the microscope. Their characteristic elements were determined and their differences from each other were shown with photographs (2).

Results: According to the results of macroscopy evaluation, flower samples meet the specifications given in the Turkish Pharmacopoeia 2017 monograph. In leaf samples, it is observed that there are other parts of the plant other than leaves in the drug package. Foreign substances were also found. The Microscopic findings obtained from the mallow leaf and flower samples in our study were presented with photographs.

Conclusions: In this study, morphological and anatomical findings obtained from the leaves and flowers of the mallow plant taken from different districts of Ankara province are given with photographs. Samples were found to be appropriate according to Turkish Pharmacopoeia 2017.

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P137
PHARMACOGNOSTICAL STUDIES ON SOME CENTAUREA L. SPECIES.

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Introduction: Centaurea species, which belongs to Asteraceae family, are widely grown all over the world and especially in the Mediterranean and Western Asia with approximately 500–900 species (1). Centaurea species have been widely used in folk medicines for centuries (2). This study aimed to evaluate the antidiabetic effects of some species of the Centaurea genus growing in Turkey and Cyprus, which are used for antidiabetic purposes in folk medicine and isolate active compound from the active species.

Materials and Methods: 70% ethanolic extracts of C. aegialophila Wagenitz, C. calcitrapa subsp. angusticeps (H.Lindb.) Meikle, C. calcitrapa L. subsp. calcitrapa, C. drabifolia Sm. subsp. cappadocica (DC.) Wagenitz, C. ensiformis P. H. Davis, C. glastifolia L., C. hyalolepis Boiss., C. iberica Trev. ex Sprengel and C. virgata Lam. were evaluated for their potential antidiabetic activities using α-amylase and α-glucosidase inhibitory activities, and the phytochemical content of these plants were analyzed to determine the compound/compounds responsible for this activity using chromatographic methods. The structures of isolated compounds have been identified by NMR technique.

Results: Hexane fraction of C. hyalolepis ethanolic extract exhibited the most powerful effect on α-amylase and α-glucosidase inhibitory activity (10.81 µg/ml and 13.11 µg/ml, respectively). Spinacetin-7-O-β-glucopyranoside, 6-methoxy-kaempferol-7-O-β-glucopyranoside, patuletin-7-O-β-glucopyranoside, apigenin, vanillic acid, 4-hydroxy-benzoic acid, 1,5-O- dicaffeoylquinic acid, isoorientin, vitexin, chlorogenic acid, arctiin, arctigenin and rafanotrachelogenin have been isolated from ethyl acetate fraction. Stigmasterol, taraxasterol and β-amyrin have been isolated from hexane fraction.

Conclusions: This study showed that alpha-amylase activity increased as it descended to the lower fractions. As a result, triterpenes, phenolic compounds, flavonoids, and lignans were determined in the extract. The antidiabetic activities of isolated compounds will be evaluated in our following studies.

Acknowledgements: This study was supported by a grant of Ankara University BAP (21L0237010)

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PHARMACEUTICAL POTENTIAL OF SALVIA PACHYSTACHYS TRAUTV. (LAMIACEAE)

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Introduction: Salvia pachystachys is a perennial species with a shrub or semi-shrub form.(1) It exhibits anticholinesterase and antidiabetic (2) properties. It was aimed to explore pharmacognostic significance of plant.

Materials and Methods: Flowers, roots, herbs methanol and aqueous extracts of each part were prepared. Essential oils were analyzed by GC-MS/MS. Antioxidant (DPPH scavenging activity, ABTS scavenging activity), total quantification (phenolic, flavonoid and tannin), antidiabetic (α-Glucosidase and α-Amylase), anticholinesterase (Acetylcholinesterase and Butyrylcholinesterase) and antimicrobial (microdilution) activities were analyzed. Safety of extracts was assessed through Ames/Salmonella and Allium test methods to evaluate biosafety.

Results: Phytol (48.4%), caryophyllene oxide (26.2%), and hexahydrofarnesyl acetone (18.3%) were main components of herb, flower, and root oils, respectively. Flower aqueous extract showed the best activity against α-amylase enzyme with 18.52% inhibition. Extracts were evaluated against α-glucosidase enzyme and no effect was observed. The highest phenolic content was determined as gallic acid equivalent with 45.777 ± 0.0004 µg GAE/mg extract value, the highest flavonoid content was determined as rutin equivalent with 282.166 ± 0.0004 µg RE/mg extract value and the highest tannin content was determined as tannic acid equivalent with 48.266 ± 0.0004 µg TAE/mg extract value. The highest DPPH and ABTS radical scavenging effect was shown by herb methanol extract. The highest % inhibition of butylcholinesterase enzyme inhibition was shown by water extract at 1000 µg/mL concentration of 15.91%, while the highest % inhibition of acetylcholinesterase enzyme inhibition was shown by root water extract. The highest antimicrobial effect was observed in root methanol extract. Extracts were evaluated as biosafe for gene and chromosome mutations up to a concentration of 1 mg/ml.

Conclusions: In conclusion, plant show promise in various pharmacological activities.

Acknowledgements: Study was supported by Ataturk University BAP (ID:13913). Enes TEKMAN thanks graduate program and scholarship supported by TUBITAK.

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DETERMINATION OF IN VITRO CYTOTOXIC ACTIVITY AND CONTENT DETERMINATION WITH HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC) OF ACHILLEA MILLEFOLIUM L. EXTRACTS

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Introduction: Achillea millefolium L. has a rich ethnopharmacological history, renowned for wound healing, appetite stimulation, and its infusion's cancer-curing properties (1,2). This study aims to explore yarrow plant extracts for cytotoxic effects, aligning with its traditional uses.

Materials and Methods: Ten different ethanol extracts (10%-99.9%) from A. millefolium aerial parts were tested on the human colon cancer cell line (Colo 205), human cervical cancer cell line (HeLa), and human breast cancer cell line (MDA-MB-231) to investigate the cytotoxic effects by using the MTT assay. HPLC analysis unveiled phytochemical content.

Results: 99.9% and 90% ethanol extracts had the lowest IC50 values in COLO 205 (52.68±2.71 and 50.63±3.12 µg/mL, respectively) and HeLa (91.46±3.00 and 97.01±7.74 µg/mL, respectively) cell lines. For MDA-MB-231, the 70% ethanol extract had the lowest IC50 (30.45±5.15 µg/mL). HPLC analysis detected chlorogenic acid, 3,5-dicaffeoylquinic acid (3,5-DCCA) (98.16 ± 2.52 µg/mL), and 3,4-dicaffeoylquinic acid (3,4-DCCA).

Conclusions: Considering Achillea L.'s medicinal potential, A. millefolium's noteworthy cytotoxicity, and its historical relevance, we continue to investigate its biological activities.

Acknowledgments: We thank the Erciyes University Research Council for providing financial support with the project code TYL-2022-11518.

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P141
UNVEILING CHEMICAL VARIANCES IN TRIGONELLAE FOENUGRAECI SEMEN FROM 5 BRANDS

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Introduction: Trigonella foenum-graecum L. is an annual plant of the Fabaceae family (1). Since ancient times, it has been used for a variety of applications such as making pastrami, a boil treatment, expectorant, appetizer, and ingredient in animal feed. Researches reveal it has various secondary metabolites such as coumarins, alkaloids, flavonoids, sterols, and saponins (2-4). Researches have also been conducted on fenugreek's antifertility, antioxidant, anticancer, antibacterial, antitumor, and antipyretic properties, as well as its capacity to inhibit the acetylcholinesterase enzyme [5]. The sources from which fenugreek seeds, which are both widely used in the community as food and as therapeutic agents and have significant activities, are obtained also carry importance. This is because there is a possibility of containing toxic substances both during collection and storage conditions. One of the most commonly encountered harmful components is pyrrolizidine alkaloids. Therefore, in this study, the chemical analyses of fenugreek seeds from 5 different commercial brands will be conducted to compare their contents.

Materials and Methods: The fenugreek seeds obtained from 5 different brands underwent initial physical inspection. Subsequently, 50 grams of each sample were subjected to maceration using an ethanol:water (1:1) solvent to prepare extracts. The chemical differences of these extracts were examined using TLC, followed by a more detailed analysis of their chemical contents using a Thermo Orbitrap Q-Exactive brand (LC/HRMS) instrument at Bezmialem Vakıf University.

Results: Upon examination of the TLC and LC-HRMS results, minor differences were observed in the chemical contents of all 5 brands, with orientin (2936.2 mg/kg) identified as the major compound in each brand. In addition to orientin, varying amounts of ascorbic acid, chlorogenic acid, naringin, nepetin-7-O-glucoside, salicylic acid, luteolin, chrysin, chrysoeriol, and hispidulin compounds were found in each extract. However, in one of the brands, a toxic compound, Seneciphylline N-oxide (5.633333 mg/kg), a pyrrolizidine alkaloid, was detected.

Conclusions: LC-HRMS data results of fenugreek seeds showed that Orientin, a flavone, was the main compound in each brand, with variations in the quantities of other chemicals. Differences in the quantities of compounds in its chemical composition are a factor that also alters the efficacy of the plant. However, only one brand was found to contain Seneciphylline N-oxide, a pyrrolizidine alkaloid known to be hazardous to both human and animal health. This indicates contamination of the plant during collection or storage. Therefore, it is important to source herbal drugs used for food and therapeutic purposes from reputable brands and known origins.

Acknowledgements: This study was supported by Bezmialem Vakıf University Scientific Research Projects Coordination Unit (Project no: BAP-20221215). We are thankful to Bezmialem İLMER for device support.

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P142
PHYTOCHEMICAL ANALYSIS AND ANTIBACTERIAL ACTIVITY OF COTA PESTALOZZAE BOISS.

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Introduction: The Cota J. Gay genus (synonymus Anthemis), previously considered a subspecies of the Anthemis species belonging to the Asteraceae family, is now recognised as a separate genus (1). It is known that the flowers of Cota species plants are used as an antiseptic (2). Among the constituents of plants of the genus Cota, flavonoids and essential oils predominate (3). The study investigated the antibacterial properties and phytochemical content of C. pestalozzae Boiss. methanol extract, an endemic species.

Materials and Methods: *C. pestalozzae* Boiss. was collected from Konya Ermenek Road on 19/05/2023 and herbarium specimens are stored in AUEF Herbarium (AEF31016). Methanolic extracts were prepared from the root and aerial parts of the plant. The extracts were analyzed by HPLC. The antibacterial activity of the aerial part extract was investigated against five different strains.

Results: According to the results of HPLC analysis, we found that the roots and aerial parts contain phenolic compounds. We observed that the roots of *C. pestalozzae* contain chlorogenic acid and 3,5-dicaffeyl quinic acid, while the aerial part contains chlorogenic acid, 4,5-dicaffeyl quinic acid, 3,5-dicaffeyl quinic acid, rutin, hyperoside and isoquercetin. This study showed that the aerial part extract exhibited antibacterial activity against *S. aureus* ATCC 43300 (MRSA). In contrast, no antimicrobial activity was observed against the other tested bacteria within the 10000-78.125 µg/ml concentration range.

Conclusions: The present study provides evidence for the antibacterial activity of *C. pestalozzae* Boiss. aerial part and the presence of phenolic compounds in both the root and aerial parts. The results of this investigation suggest that *C. pestalozzae* Boiss. could be a potential source of natural antibacterial agents. Further research is needed to isolate and identify the compounds to reveal the plant's phytochemical structure.

Acknowledgements: Declared none.

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P143
ISOLATION AND IDENTIFICATION OF SECONDARY METABOLITES FROM TRAGOPOGON COLORATUS C. A. MEY.

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Introduction: Tragopogon L. belongs to the Asteraceae family and is widely distributed in Europe and Asia with around 110 species. The genus Tragopogon, is represented by 20 species in the European flora, 79 species in Russia, and 37 species in the Iranian flora, and in our country, 18 species belonging to the genus Tragopogon were recorded according to Matthews (1975) (1), that the number reached 25 with the recently described taxa. (2-4). Seven of these taxa are endemic to Turkey and the endemism rate was determined as 33% (3). This study aims to isolate and determine the structure of new compounds from the plant's aerial parts by performing a detailed phytochemical examination on the selected Tragopogon coloratus C. A. Mey., on which no isolation studies have been carried out to date. T. coloratus is known as "renkli yemlik" in folk medicine and its aerial parts are edible.

Materials and Methods: The phytochemical content of the T. coloratus ethyl acetate fraction was obtained from the aerial parts of total methanolic extract using liquid-liquid fractionation from herbal material through maceration processes. The obtained ethyl acetate fraction was separated using column chromatography on C-18 with methanol: water (2: 3) solvent system. The obtained ethyl acetate fraction was combined and the compounds were purified by semi-prep HPLC and prep-TLC using reverse-phase TLC plates.

Results: Genkwanin-5-O-β-glucoside, orientin, isoorientin, vitexin, chlorogenic acid, 4,5 di-O-caffeoylquinic acid, 3,5 di-O-caffeoylquinic acid and their methyl ester as well as dihydrostilbene derivatives which are still under structure elucidation were isolated. The structures of the compounds were established using spectrophotometric methods such as 1H- and 13C-NMR, 2D-NMR and MS analyses.

Conclusions: As a result, phytochemicals were isolated in the T. coloratus. The biological activities of isolated compounds will be evaluated in our following studies.

Acknowledgements: Declared none.

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P145
EFFECT OF MELISSA OFFICINALIS ON C. ELEGANS THERMOTOLERANCE

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Introduction: Caenorhabditis elegans (C. elegans) is a commonly used biological model organism thanks to its short life cycle/span, small size, transparency, defined genome etc. (1). Leveraging the advantages offered by this microscopic worm, our study aimed to investigate the potential ameliorative effects of Melissa officinalis MeOH extract on the toxicity of benzo[a]pyrene (BaP) an environmental pollutant (2).

Materials and Methods: Once the worms were synchronized, the eggs were moved to petri dishes with a concentration of 20 M BaP. Following a 24-hour exposure period, the organisms were retrieved using M9 buffer, rinsed, and subsequently transferred to petri dishes with varying quantities of extract (1.2 mg/ml, 0.6 mg/ml, 0.36 mg/ml, and blank as a control). Following the 24-hour treatment, the petri dishes were moved to a 35oC incubator for the purpose of conducting a thermotolerance assay as a short-term lifespan analysis experiment (3). The organisms were then monitored until their death. All groups were studied in triple.

Results: According to our findings, mortality rates were dose-dependently increased by M. officinalis extract after BaP exposure. Significant differences between experimental and control groups were highlighted by statistical analyses, emphasizing the need for further research on potential anthelminthic activity of M. officinalis.

Conclusions: The study found no evidence of antioxidant or restorative properties exhibited by the extract towards living organisms. Antihelminthic activity of the extract against living organisms has been demonstrated at the studied concentrations.

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P146
CYTOTOXIC ACTIVITY INVESTIGATION OF HERACLEUM SPHONDYLIUM SUBSP. CYLOCARPUM (C. KOCH) DAVIS

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Introduction: Species of the genus Heracleum L., belongs to Apiaceae, which comprises 120 species worldwide, is distributed in our country with 21 taxon (1). 6 of these taxa are endemic to Turkey. Heracleum species contain phenolic compounds, especially coumarin compounds. Coumarin and its derivatives exhibit various biological activities, including anticancer properties (2). This study aims to investigate the cytotoxic activity of petroleum ether, dichloromethane and methanol extracts of Heracleum sphondylium subsp. cyclocarpum.

Materials and Methods: The extracts of the aerial part of the plant were obtained by percolation method with petroleum ether, dichloromethane and methanol. All extracts were investigated for their cytotoxic activity against MDA-MB-231 (breast cancer cell line), C6 (glioma cancer cell line) and NIH-3T3 (embryonic fibroblast; non-cancerous cell line) cell lines by XTT method. A concentration that kills 50% of the cells (IC50) was determined and used to compare the activity of different extracts.

Results: According to the results; the dichloromethane fraction is most active extract with 28.76 µg/mL IC50 value on MDA-MB-231 cell line. The petroleum ether fraction is most active extract with 28.13 µg/mL IC50 value on C6 cell line.

Conclusions: The petroleum ether extract of H. sphondylium subsp. cyclocarpum was found to have the highest cytotoxic effect. It was determined that the petroleum ether and methanol extracts of the plant did not have a toxic effect on healthy cells (NIH-3T3). These extracts can be promising for future cytotoxic activity-guided isolation studies.

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P147
EVALUATION OF THE COMPLIANCE OF DANDELION SAMPLES SOLD IN HERBALISTS AND ON THE INTERNET ACCORDING TO THE TURKISH PHARMACOPOEIA

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Introduction: Taraxacum officinale F.H. Wigg (Asteraceae) has been used in folk medicine to treat eye diseases, wounds, animal bites, stomach and liver diseases, kidney stones, hepatitis, cancer, bacterial infections, cold and flu, hypertension, rheumatism and also as diuretic (1). Dandelion roots and leaves contain major compounds such as flavonoids, phenolic acids, coumarins, terpenoids, carotenoids and phytosterols (2). Aim of the study is to evaluate the compliance of dandelion samples sold in herbalists and on the internet.

Materials and Methods: Macroscopical and microscopical examination, thin layer chromatography, loss on drying and total ash determination were performed on twelve dandelion samples obtained from herbalists and on the internet in accordance with the section under the title "Taraxaci officinalis herba cum radice" in Turkish Pharmacopoeia.

Results: It has been found adulteration in some samples according to the macroscopical and microscopical examination. Thin layer chromatography revealed that some samples did not contain the compounds specified in the Pharmacopoeia. While loss on drying test showed that three samples exceeded the limit value; total ash test showed that half of the samples were above the pharmacopoeia limit value.

Conclusions: When the results of the tests are evaluated, it is seen that not all samples obtained from herbalists and websites meet the requirements specified in the Turkish Pharmacopoeia.

Acknowledgements: This study was supported by a grant of TUBITAK (2209-A).

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P148
ENZYM INHIBITORY, ANTIOXIDANT ACTIVITES AND PHYTOCHEMICAL STUDIES ON *STACHYS CRETICA* L.

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Introduction: Stachys cretica L. (Lamiaceae) is a plant that grows in Turkey and is used for medicinal purposes and is known as Deliçay (1). In this study, we aimed to evaluate the in vitro antidiabetic, antiobesity, antihyperlipidemic and antioxidant activities of the extract prepared from the aerial part of the S. cretica plant.

Materials and Methods: The aerial part of S. cretica was collected from Ankara in June 2023. α-Amylase, α-glucosidase, pancreatic lipase and pancreatic cholesterol esterase inhibitory effects and antioxidant activities were evaluated on the methanol extract of the plant. The antioxidant activities of the extracts were determined by DPPH radical scavenging, ferric reducing and metal chelating capacity. In addition, the total phenol and flavonoid contents of the extract were also investigated (2).

Results: As a result of the study, the inhibition of the extract at a concentration of 200 µg/ml on both α-glucosidase and α-amylase enzymes was over 50% and was calculated as 73.27 ± 1.51% and 50.43 ± 3.53%, respectively. The extract has no inhibition on the pancreatic lipase enzyme. It had an inhibition value of 46.93 ± 1.48 % on the pancreatic cholesterol esterase enzyme at a concentration of 200 µg/ml, close to the reference substance simvastatin (66.63 ± 2.52%). In all three methods where antioxidant capacity was evaluated, the extract had values very similar to the reference substances. Additionally, the extract was found to have remarkable content in terms of phenolics (91.25 ± 9.14 mg gallic acid equivalent/g extract) and flavonoids (22.53 ± 0.31 mg quercetin equivalent/g extract).

Conclusions: It has been determined that the aerial parts of S. cretica may be a natural source of antidiabetic, antihyperlipidemic and antioxidant activity that can be subject to in vivo research.

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P149
RESVERATROL AND POLYDATIN CONTENT OF CULTIVATED SIX DIFFERENT PEANUT VARIETIES FROM TÜRKİYE

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Introduction: Arachis hypogaea L., commonly known as peanut is one of the cultivated plant belongs the Fabaceae. The different parts of the plant contain various phytochemicals like phytosterols, anthraquinones, phenolics, resveratrol, and its glycoside, polydatin. A stilbenoid, resveratrol has been detected in the shells, leaves and roots of peanuts, especially in their seeds. Polydatin is also found in various organs of peanuts. In addition to having strong antioxidant activity, these two valuable secondary metabolites also have cardioprotective, antiinflammatory, neuroprotective, antiatherosclerotic and immunoregulatory activities (1-3). Our study was aimed to determine the resveratrol and polydatin amounts especially in the waste parts of the plant in the roots and shells.

Materials and Methods: The resveratrol and polydatin content of the six peanut varieties grown in Hatay were determined using High Performance Liquid Chromatography (HPLC)-DAD. The roots and shells, which are typically considered waste after harvesting, were extracted using Ethanol:Water (80:20) at three different conditions: 40°C, 70°C, and in a microwave at 70W. All extracts and standard pure compounds resveratrol and polydatin were applied to the validated HPLC-DAD system.

Results: The analysis revealed that the shell extract of the "Efsane" variety prepared at 40°C had the highest yield of polydatin (0.85 mg/g), while the shell extract of the "Masal" variety prepared at 70°C had the highest yield of resveratrol (0.84 mg/g).

Conclusion: Our study demonstrates the potential of utilizing peanut waste, specifically roots and shells, as a valuable source of bioactive compounds. The findings suggest that extraction conditions significantly affect the yield of resveratrol and polydatin, highlighting the importance of optimizing extraction processes for maximizing the recovery of these beneficial compounds.

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P150
POTENTIAL NEUROPROTECTIVE ACTIVITY OF HALICLONA (RHIZONIERA) SARAI (PULITZER-FINALI, 1969)

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Introduction: Marine ecosystems, characterized by rich biodiversity and unique environmental conditions, have long been recognized as a prolific source of compounds exhibiting various biological activities. The exploration of marine organisms has led to the discovery of compounds with potential therapeutic and industrial applications, including antimicrobial, anticancer, anti-inflammatory, and neuroprotective properties (1–3). Haliclona (Rhizoniera) sarai (Pulitzer-Finali, 1969), a species of marine sponge belonging to the family Chalinidae, is known for its unique morphology and ecological significance in marine ecosystems. Recent research in the seas of Turkey has reported its presence in the Levantine Sea (4), the Sea of Marmara (5), the Dardanelles (shipwreck) (6), and the Aegean Sea coasts (4, 6). It is evident that studies specific to this species in Turkish waters are quite limited. Within the scope of this study, H. (R.) sarai, scientifically sampled from the deep water zone off the coast of Gökçeada, represents a new record for the sponge fauna of Gökçeada (7). Alzheimer's disease presents cognitive decline and memory loss challenges. Cholinesterase inhibitors promise symptom alleviation by enhancing cholinergic neurotransmission. Natural products, crucial in Alzheimer's research, offer diverse structures for potent inhibitors, with multifaceted pharmacological properties including antioxidant and neuroprotective effects, potentially leading to safer and more effective treatments, thus improving patient outcomes. Studies have shown that 3-alkylpyridinium salts that obtained from aqueous extracts of H. (R.) sarai sponges contain, which exhibit strong acetylcholinesterase inhibitory activity (8). However, there is a lack of data regarding the apolar extracts.This study aims to investigate the acetylcholinesterase inhibitory activities of the hexane and dichloromethane:methanol (1:1) extracts of H. (R.) sarai sponges.

Materials and Methods: H. (R.) sarai, scientifically sampled from the deep water zone off the coast of Gökçeada. Samples were frozen at -80 0C, subsequently dried using the lyophilization method, and then ground in a blender. Hexane and Dichloromethane-Methanol (1:1) extracts were prepared from the ground samples using the maceration method. The anti-Alzheimer activities of the prepared extracts were analyzed by in vitro acetylcholinesterase inhibitory activity tests according to the Ellman method (9).

Results:

	Concentration					
	200	**100**	**50**	**25**	**12,5**	**IC_{50}**
Galantamin	80	77	75	72	67	0.55±0.01
HS-Hexane extract	17	15	12	10	9	>200
HS-DCM:MeOH extract	55	47	31	22	10	**136.30±0.02**

Conclusions: In vitro Anti-Alzheimer activity of the H. (R.) sarai Hexane and DCM:MeOH (1:1) extracts was investigated for the acetylcholinesterase enzyme inhibitory activities according to the Ellman's method and was compared with galantamine as a standard. According to the IC50 values, the Anti-Alzheimer effect of the sponge extract is found more efficient for H. (R.) sarai DCM:MeOH (1:1) extract.

Acknowledgements: This study financially supported by Bezmialem Vakif University, Scientific Research Project Number: BAP 20240214

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P151
BIOLOGICAL ACTIVITIES OF VITIS VINIFERA L. (ANTEP KARASI) SEED OIL

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Introduction: Vitis vinifera L., is a species of Vitaceae family, traditionally used for medicinal properties. The seed oil is also known as "royal oil" and widely used in various industries, including culinary, pharmaceutical, cosmetic, and medical purposes (1-4). The aim of this study was to investigate V. vinifera seed oil for biological effects and chemical composition.

Material and Methods: The seeds were collected from the grapes famous as "Antep karası" and growing locally in Gaziantep province of Turkey. The seeds have been extracted with n-hexane in a Soxhlet apparatus to get the oil. The chemical composition of the oil was analyzed with GC- FID/MS after transesterification of the fatty acids with BF3 reagent. The total phenol and flavonoid contents were determined spectrophotometrically. The oil was tested for antioxidant activity with DPPH assay and β-carotene bleaching test. The antimicrobial activity of the oil was determined against Gram (+), Gram (-) and Candida species using broth microdilution method.

Results: The seed oil yield was calculated as 8.2%. The scavenging property against DPPH free radicals was determined as IC50 1.42±0.004 mg/mL. The inhibition value in the β-carotene bleaching test was obtained as 0.18±0.02 mg/mL. The total phenol content was found to be 0.07±0.01 mgGAE/g. The total amount of flavonoids was determined as 0.02±0.001 mgRE/g. The MIC values of the seed oil ranged from 0.23 to 15.0 mg/mL. The oil was found to be ineffective on Gram (+) bacteria cultures.

Conclusion / Discussion: The study reveals that "Antep karası" seed oil can be considered as a promising source for antioxidants with low MIC values, highlighting the need for further research on its overall activities.

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P152
EFFECT OF NANOTECHNOLOGY-BASED DRUG DELIVERY SYSTEMS ON THE BIOLOGICAL ACTIVITY OF CARVACROL

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Carvacrol, with its biological and pharmacological activities, is currently used in many fields such as the pharmaceutical industry, cosmetics industry and veterinary medicine (Umran et al., 2022). These activities can be listed as antimicrobial, antitumor, antigenotoxic, analgesic, antispasmodic, antiinflammatory, angiogenic, antiparasitic, antiplatelet, antielastase, insecticidal, antihepatotoxic and hepatoprotective activities (Baser, 2008).

However, carvacrol's pungent odor, volatile nature, low water solubility, oxidative degradation and irritating nature create disadvantages to use. For this reason, carvacrol is loaded into nano-drug carrier systems, and its stability is ensured, negative properties are avoided (Ayres et al., 2020). Nanostructures as drug delivery systems have increased or protected the biological activity of carvacrol by eliminating the disadvantages of its use.

In this study, articles in the literature about drug carrier systems containing the carvacrol molecule were examined. In those studies, nanoparticles were mostly preferred for the carvacrol molecule, and most of carvacrol-containing encapsulation studies focused on the antimicrobial activity, and its effect on bacteria and fungi was tried to be increased and maintained by encapsulation, and successful results were achieved. The remaining studies focused on increasing antitumoral activity and antioxidant activity and examined its effects on arthritis and cancer pain. In all of these studies, nanoemulsions, nanoparticles and liposomes come first as drug carrier systems. However, it is important to expand these studies with carvacrol with clinical trials. More studies are needed to elucidate the pharmacokinetic properties and side effect profile of carvacrol.

Keywords: carvacrol, nanoparticles, encapsulation, polymer

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P153
PHYSICIANS' AWARENESS ON THE SAFETY OF HERBAL PRODUCTS.

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Introduction: The use of herbal products among the population is becoming more common in Turkiye. In accordance with this, it is noted that the number of adverse effects associated with the use of herbal products is increasing. Phytovigilance, or phytopharmacovigilance, is defined as the detection, evaluation, and prevention of adverse reactions and other potential problems associated with the use of herbal products (1,2). It is very important for physicians who are responsible for following the treatment of patients to identify and report the side effects of herbal products. This study aimed to determine, the awareness of physicians about the phytovigilance system and the factors affecting this awareness, for the first time in Turkiye.

Materials and Methods: The descriptive study was conducted at Karadeniz Technical University Farabi Hospital between November 1, 2023 and February 1, 2024, by using the face-to-face interview technique. It was a survey, including two main sections and 21 questions. The statistical analysis was performed with SPSS 23.0. The combined effects of all possible variables, which might be associated with phytovigilance awareness, were assessed by binary logistic regression analysis using the Backward LR elimination method. The $p<0.05$ indicates the significance level.

Results: Among 268 survey responses in the study, 56.7% of the participants were male, and 66.8% were working in internal medicine. The mean work experience was 6.6 ± 7.7 years. Among the participants, 45.5% had heard of the concept of phytovigilance. 69.8% of respondents did not know that adverse reactions related to the use of herbal products were reported in Türkiye. Among those who were aware of the feedback process, 70.4% did not know that hepatotoxicity and nephrotoxicity notification forms were filled out in the feedback. Only 27.2% of physicians knew that there was a phytovigilance contact point in the hospital where they worked. It was determined that the factors that enhance phytovigilance awareness were being a specialist physician [Odds ratio (OR) = 4.591; p = 0.001], knowing that adverse effects related to herbal products were reported feedback (OR = 2.678; p = 0.001), and questioning the use of herbal products while taking the medical history of patients (OR = 3.522; p = 0.012).

Conclusions: It was revealed that the knowledge of the physicians about the phytovigilance system in Turkiye was quite low. To improve awareness, information campaigns on the phytovigilance system should be organized in hospitals, and the process of ensuring the safety of herbal products should be integrated into the curricula of undergraduate medical faculty.

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P154
EVALUATION OF ANTIOXIDANT AND ANTIMICROBIAL ACTIVITIES OF TEUCRIUM SANDRASICUM AND TEUCRIUM DIVARICATUM SUBSP. GRACEUM

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Introduction: Teucrium species are commonly used as diuretics, antiseptics and anti-helmintics, as well as in the treatment of diabetes, stomach ulcers and intestinal inflammation. In this study, it is aimed to assess the phenolic content, as well as the antioxidant, and antimicrobial activities of infusion, methanol, ethanol, and n-hexane extracts from T. sandrasicum O. Schwarz and T. divaricatum subsp. graecum (Celak.) Bornm. aerial parts.

Materials and Methods: T. sandrasicum (TS) and T. divaricatum subsp. graecum (TD) were collected from Muğla province. The extracts were obtained by macerating aerial parts of the plant materials for 3x24h using methanol, ethanol (E) and n-hexane (H). Furthermore, 5% infusion samples were made. The total phenolic content of the extracts was evaluated using the Folin–Ciocalteau reagent and determined according to the method of Gao et al (2). The in vitro DPPH and ABTS radical scavenging activity of the extracts were determined by the protocol applied by Goger et al. (3). The MIC values of the strains were determined by broth microdilution methods (4).

Results: The total phenolic content for both plants was found to be higher in methanolic extracts compared to the others (TD 107.8 mg GAE/g ext- TS 98.4 mg GAE/g ext). Antioxidant activity results revealed that the inhibition percentage of methanol extracts obtained from both plants was high in DPPH and ABTS tests. According to the antibacterial activity test results, obtained from MIC tests the extracts were found not to be very active against the identified microorganisms compared to the control.

Conclusions: According to the study results, it was determined that Teucrium extracts have positive antioxidant activities and can be a source of natural antioxidant components.

Acknowledgements: This study was supported by Scientific Research Coordination Unit of Anadolu University under the project number 2207S090.

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P155
HS-SPME/GC/GC-MS ANALYSIS OF VOLATILE CONSTITUENTS OF LEONURUS L.

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Introduction: Leonurus species, known as "Motherwort", are used as an herbal remedy for relaxation and calmness. It also often has tonic effects on the neurological, hormonal and cardiac systems. (1, 2). The genus Leonurus is represented in our country by 4 species (L. cardiaca L., L. glaucescens Bunge, L. persicus Boiss., L. quinquelobatus Gilib.). Essential oil (EO) and HS-SPME studies of Leonurus species grown in Türkiye have not been reported in the literature. The aim of the current study is the characterization of volatile components obtained from the aerial parts of Leonurus species using HS-SPME/GCFID/GC-MS.

Materials and Methods: Four species were collected as flowering and fruity from Kocaeli, Edirne, Bursa, Bolu, and Erzurum localities. Essential oil was obtained from the aerial parts of Leonurus species using Eppendorf Microdistiller®. GC-GC/MS analysis of essential oils obtained by microdistillation was performed with the Agilent 5975 GC-MSD system. For HS-SPME analysis on plant materials was performed using SPME fiber PolydimethylsiloxaneDivinylbenzene (PDMS/DVB-65um)-Blue.

Results: The major constituents of the essential oil of L. glaucescens and L. persicus species were identified as α-pinene and p-cymene, whereas in L. quinquelobatus the major components are p-cymene, 1,8-cineole, and germacrene D. β-caryophyllene and α-humulene were found to be the main compounds in the L. cardiaca species.

Conclusions: The obtained results are compatible with the essential oil profiles of different parts of various Leonurus species found in the literature. The present work is the first contribution into the volatile constituents of Leonurus from Türkiye.

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P156
ANTIOXIDANT AND ANTIMICROBIAL ACTIVITIES OF BALLOTA NIGRA L. SUBSP. ANATOLICA DAVIS

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Introduction: B. nigra L. known as "yalancı ısırgan" in our country, is used to cure gut disorders, prevent nausea and vomiting, and exhibit sedative characteristics in situations of anxiety and tension (1,2). Its aerial parts are utilized as infusions, liquid extracts, or tinctures (2). Plants secondary metabolites have extensively different bioactivity properties. In this study, methanol, ethyl acetate extracts and infusion samples of the aerial parts of B. nigra subsp. anatolica were prepared, and their antimicrobial and antioxidant effects were examined.

Materials and Methods: B. nigra subsp. anatolica was collected from Çanakkale, Türkiye. Extracts were obtained from the aerial parts of the plant using methanol and ethyl acetate. A 5% infusion sample from the aerial parts of the plant. The antioxidant effects of the species were determined by the DPPH˙ method, and the total phenolic content was determined in terms of gallic acid equivalent by the Folin-Ciocaltaeu method. To monitor antimicrobial activity, the methanol, ethyl acetate extracts and infusion samples of B. nigra subsp. anatolica were determined against Gram-positive (Stapylococcus aureus ATCC 29213, Bacillus cereus NRRL B-3711, Listeria monocytogenes ATCC 19111), Gram-negative (Pseudomonas aeruginosa ATCC 27853) and Candida species (C. albicans ATCC 90028, C. krusei ATCC 6258) by the broth microdilution method.

Results: As per the findings, the B. nigra subsp. anatolica methanol extract has the most amount of total phenol (66.8±0.01 mg GAE/g ext). The methanol extract of the plant exhibited higher antioxidant activity than other extracts, with an IC50 value of 0.516 ±0.02 mg/ml. The most effective extract was the methanol extract, followed by infusion (IC50: 0.613±0.03 mg/ml). By using broth microdilution method, Minimum Inhibitory Concentration (MIC) values were determined. The MIC values of methanol and ethyl acetate extracts varied between 97-3125 µg/mL. When a comparison is made between standard bacteria and yeast species based on MIC values, it can be interpreted that yeast species are more sensitive to plant extracts than bacteria species with low MIC values.

Conclusions: This study aims to shed light on the biological properties of B. nigra subsp. anatolica, a medicinal plant in Türkiye. The results revealed the correlation between phenolic compounds and antioxidant activity. Additionally, methanol and ethyl acetate extracts of the plant showed significant antimicrobial activity to both standard bacteria and yeast cultures.

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P157
EXAMINATION OF MORPHOLOGICAL AND ANATOMICAL FEATURES ON 3 GENISTA SPECIES GROWING IN TÜRKİYE

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Introduction: The genus Genista L. belongs to the family Fabaceae (Leguminosae). The genus Genista includes a total of 144 species. There are 16 Genista taxa growing in Türkiyeand 6 of them are endemic. Genista species, commonly known as "borcak" in our country, are traditionally used internally for diuretic and external anti-inflammatory purposes. In studies conducted on Genista taxa, it has been determined that plants exhibit various biological activities such as hypoglycemic, spasmolytic, antioxidative, anti-inflammatory, antimicrobial, diuretic, antiulcer, hepatoprotective and estrogenic activities. In this study, morphological and anatomical studies were carried out on the stems and leaves of three different Genista species (Genista acanthoclada DC., Genista januensis Viv. subsp. lydia (Boiss.) Kit Tan & Ziel. and Genista involucrata Spach (endemic)) (1-4).

Materials and Methods: The plant materials used in this study were collected from various parts of Türkiye. Samples were taken from the aboveground parts of the plants (the stem and leaves) and herbarium samples were prepared and registered at Ankara University Faculty of Pharmacy Herbarium (AEF) and placed in cabinets. For anatomical studies, cross-sections were taken from stem and leaf samples stored in 70% ethanol. For cross sections, preparations were prepared with Sartur and chloral hydrate reagents. Schematic examinations were performed with 10x4, 10x10 magnification; and anatomical examinations were performed with 10x40 magnification. LEICA CME microscope was used for microscopic examination of the samples.

Results: In this study, the leaves and stem parts of 3 species of the Genista genus that grow naturally in our country were examined morphologically and anatomically and their structures were clarified.

Conclusions: The features of these structures are given in detail with photographs. The differences in the morphological and anatomical structures of the 3 species examined were determined.

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P158
APIGENIN AND HOMOGENTISIC ACID PROTECT AGAINST B[A]P INDUCED GENOME DAMAGE IN LUNG CANCER (A549) CELLS

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Introduction: Benzo[a]pyrene (B[a]P), a polycyclic aromatic hydrocarbon, is one of the main air pollutants, and although designated by the International Agency for Research on Cancer (IARC) as a human carcinogen (Group 1), its mechanisms of action are still not fully understood. Its metabolites can cause specific mutations in the p53 tumour suppressor gene and DNA adducts in human bronchial epithelial cells, thus providing a direct link between lung cancer and B[a]P exposure. A549 cells have retained some metabolic activities of the normal type II alveolar cells (expressing CYP1A1, CYP1B1 and CYP2B6), making them a valuable model for lung damage effects and possible lung cancer development. Here we aimed to assess primary, oxidative and permanent DNA damage in A549 after 24 and 48 h exposure to the environmentally relevant B[a]P concentrations (1,2,5,10,20,50,60 μM), and to investigate the protective role of antioxidant homogentisic acid (HO, Arbutus unedo (strawberry-tree honey) and apigenin (API, a dietary flavonoid).

Materials and Methods: Cytotoxic and proliferative effect was evaluated by the MTT assay. DNA strand breaks and oxidatively damaged DNA were assessed using the alkaline and Fpg-modified comet assays. Micronucleus (CBMN) cytome assay was used for the evaluation of chromosomal damage and proliferation kinetics. Besides, we used a wound-healing assay to evaluate the cell invasion effect.

Results: Primary DNA damage did not significantly differ among treatments in both periods while we observed oxidatively damaged DNA after 24 h of exposure. CBMN assay revealed that even the lowest B[a]P concentrations demonstrated induction of apoptosis along with the increased frequency of micronuclei and nuclear buds indicating dose-dependent genome instability. Both HO and API demonstrated a protective effect, for all API concentrations tested, and only for the lower HO concentration corresponding to the one cup of tea daily, and lower B[a]P concentrations. Besides, API and HO stopped or slowed the wound repair time whilst lower B[a]P concentrations repaired the wound faster (usually within 24 h) and higher concentrations needed a longer time for the same observed effect (72 h).

Conclusions: Both API and HO demonstrated their protective effects but using different pathways. Lower B[a]P concentrations, readily present in the outdoor air, demonstrated different effects than higher ones, and stronger wound healing effects. These observations point out that the effect of continuous exposure to low B[a]P concentrations can be more dangerous for the lung cells than the exposure to the higher ones, warranting further research.

Acknowledgements: Supported by the European Regional Development Fund project KK.01.1.1.02.0007 (Rec-IMI), the Croatian Science Foundation (HUMNap project #1192), the Horizon Europe (EDIAQI project #101057497), the European Union—Next Generation EU 533-03-23-0006 (BioMolTox) and Erasmum programme 82271-Preparazione prova finale all' Estero.

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P159
ANTICANCER ACTIVITY OF CENTAUREA GLASTIFOLIA L. (ASTERACEAE) LEAF EXTRACT ON A549 CELL LINE

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Introduction: Centaurea L. species have shown significant biological activities such as wound healing, easing inflammation and rheumatoid arthritis (1, 2). They are a rich source of phytochemicals that exhibit several activities including anticancer, antiinflammatory and antioxidant (3). The current study was conducted to explore the anticancer activity of C. glastifolia L. leaf extract.

Materials and Methods: The study used the human lung adenocarcima cell line A549 for a MTT assay. The cells were incubated in Dulbecco's Modified Eagle Medium (DMEM) and plated into 96-well microtiter tissue culture plates. The optimum cell number for cytotoxicity assays was determined. Stock solutions of compounds were prepared. The level of cellular 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) reduction was quantified. The formazan crystals formed by MTT metabolism were solubilized, and absorbance was measured.

Results: While cisplatin has expressed 11.21% of early apoptosis, C. glastifolia has expressed 3.27% of early apoptosis. While cisplatin has expressed 15.31% of late apoptosis, C. glastifolia has expressed 37.22% of late apoptosis.

Conclusions: C. glastifolia has shown a significant anticancer effect on the A549 cell line. Early and late apoptosis results of C. glastifolia were found to be higher than those of cisplatin. The next step is to determine and isolate the active compound that is responsible for the effect. Further studies will focus on investigating the mechanism of action of this compound.

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P160
CHEMICAL COMPOSITION AND CYTOTOXIC ACTIVITIY OF ENDEMIC *ORIGANUM SIPYLEUM* L.

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Introduction: The genus Origanum L., which belongs to the Lamiaceae family, is represented by 6 hybrid and 25 taxa in the flora of Turkey. Origanum sipyleum L. is a widespread endemic species, known as "Mor mercan" in Turkey (1). The aim of this study was to investigate the chemical composition and cytotoxic activity of the infusion and extracts of O. sipyleum (OS).

Materials and Methods: Plant materials were collected from Denizli in June, 2021. Air-dried and powdered aerial parts of OS were extracted with n-hexane, EtOAc, and MeOH, sequentially, and also total EtOH (ultrasound assisted-UA and soxhlet) extracts and infusion were prepared. In this study, the chemical compositions of the infusion and extracts were determined by HPLC analysis. The cytotoxic activity of samples of OS were evaluated on human lung (A549), human breast cancer (MDA-MB-231), human melanoma (SK-MEL-30), and human prostat cancer cell lines (PC-3) using MTT (3-(4,5-dimethylthiazol-2yl)-2,5-diphenyltetrazolium bromide) assay .

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Results: HPLC analysis demonstrated that the infusion and extracts contained variable amounts of rosmarinic acid (282.84-601.53mg/100g dry herb) and hyperoside (4.58-85.94mg/100g dry herb). In this study, OS-EtOAc extract showed strongest cytotoxic activity against whole cell lines. According to the results, OS-EtOAC extract decreased cell viability by 62.27%, 47.37%, 55.18% and 80.71% on A549, MDA-MB-231, SK-MEL-30 and PC-3 cell lines, respectively. In addition, the IC50 value of OS-EtOAc extract on the PC-3 cell line was 90.49±19.78 µg/ml.

Conclusions: To the best of our knowledge, this is the first report on the cytotoxic activity of O. sipyleum on A549, MDA-MB-231, SK-MEL-30 and PC-3 cell lines.

Acknowledgements: This study was supported by a grant of TUBITAK 2209/A- University Students Research Projects Support Program.

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CHEMICAL COMPOSITION AND ANTIMICROBIAL ACTIVITY OF SIDERITIS LIBANOTICA LABILL. SUBSP. KURDICA (BORNM.) HUB.-MOR.

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Introduction: The genus *Sideritis* L., which belongs to the Lamiaceae family, is represented by 45 species and 53 taxa in the flora of Turkey. *Sideritis libanotica* Labill. subsp. *kurdica* (Bornm.) Hub.-Mor. is a widely distributed taxon, locally known as "İnce çay" (1). The aim of this study was to determine the chemical composition and antimicrobial activity of *S. libanotica* subsp. *kurdica* (SL) collected from Turkey.

Materials and Methods: Plant materials were collected from Mt. Nemrut (Adiyaman) in June, 2021. The voucher specimen were deposited in Herbarium of Ege University, Faculty of Pharmacy, Izmir, Turkey (IZEF NO: 6028). In this study, air-dried and powdered aerial parts of SL were extracted with n-hexane, EtOAc, and MeOH, sequentially, and also total EtOH (both ultrasound assisted and soxhlet) extracts and infusion were prepared. The phytochemical composition of the extracts were determined by HPLC analysis. Antimicrobial activity of extracts were tested against three Gram-negative (Escherichia coli, Salmonella typhimurium and Pseudomonas aeruginosa) and two Gram-positive (Staphylococcus aureus and Enterococcus faecalis) pathogenic bacteria by microdilution methods.

Results: HPLC analysis showed that the extracts contained variable amounts of chlorogenic acid (22.00-100.91mg/100g dry herb), verbascoside (4.66-114.50mg/100g dry herb) and rosmarinic acid (20.10-160.92mg/100g dry herb) were determined in extracts. According to the results, the infusion and ethanol extracts showed strongest antimicrobial activity (MIC: 187.5 µg/mL) against E. faecalis among all samples tested.

Conclusions: To the best of our knowledge with this study, the antimicrobial activity of S. libanotica subsp. kurdica was investigated first time.

Acknowledgements: This study was supported by a grant of TUBITAK 2209/A- University Students Research Projects Support Program.

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P162
AN ETHNOMEDICINAL STUDY IN ÇANKIRI (TÜRKİYE)

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Introduction: Çankırı province located in the north of Central Anatolia, is a transition zone between Irano-Turanian and Euro-Siberian phytogeographical regions. In this study, biological resources used in traditional medicine in Çankırı province were investigated within the scope of the Recording Traditional Knowledge Based on Biological Diversity Project.

Materials and Methods: Field studies were carried out in 40 villages of 12 districts of Çankırı between 2022-2023, and the ethnomedicinal data was collected through semi-structured face-to-face interviews with the local people. The plant materials collected during the field studies were identified using Flora of Turkey (1, 2). The voucher specimens were deposited in the Herbarium of Hacettepe University, Faculty of Pharmacy, Ankara, Turkey (HUEF). In addition, the use value (UV) and Informant consensus factor (FIC) values of the plants were calculated.

Results: In this study, ethnomedicinal data was obtained from 102 of the 245 people interviewed. It was determined that 37 wild species (30 plant species belonging to 18 families and 7 animal species belonging to 7 families) were used in traditional medicine in Çankırı. The most commonly used plant species were found as Pinus nigra J.F. Arnold (UV: 0,53), Malva neglecta Wallr. (UV: 0,41), and Plantago major L. (UV: 0,25), respectively.

Conclusions: Traditional medicinal knowledge holds significant cultural value. This study highlights that in Çankırı province, a considerable portion of this heritage is disappearing without being transferred to the next generations.

Acknowledgments: This study was supported by the Republic of Turkey, Ministry of Agriculture and Forestry, General Directorate of Nature Conservation and National Parks.

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P163
FERULIC ACID: CANNABINOIDERGIC SYSTEM IS PARTIALLY INVOLVED IN ANALGESIC EFFECT IN INFLAMMATORY PAIN

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Introduction: Pain is a psychological, physical or emotional sensation that may be associated with tissue damage and inflammation (1). The most commonly used drugs for pain are non-steroidal anti-inflammatory drugs (2). It is observed that frequent use of analgesics leads to various side effects in individuals. These difficulties have led scientific researchers all over the world to search for alternative treatment. Herbal origin medicines are considered as an alternative treatment and used in a wide range of diseases such as pain and inflammation with little or no side effects (3). The goal of this study is to investigate the analgesic effect of ferulic acid, a natural antioxidant phenolic, and the role of cannabinoidergic system in its effect in capsaicin-induced inflammatory pain.

Materials and Methods: To induce inflammatory pain, 20 µg capsaicin was administered in a volume of 20 µL by intraplantar route. To test the effect of ferulic acid; 150, 300 and 600 µg doses of ferulic acid were administered, intraplantar route (in a volume of 30 µL) 15 min before the capsaicin injection. For mechanism of action studies; CB1 receptor antagonist AM251 was administered i.p. at the dose of 10 mg/kg and CB2 inverse agonist AM630 was administered i.p. at the dose of 10 mg/kg. All pain thresholds were measured at 0-180 min time interval with an electronic von Frey device.

Results: As a result of the study, a decrease was observed in the pain thresholds of animals given capsaicin. In animals injected with ferulic acid, a significant increase in pain thresholds was observed at all doses and time points tested. Pretreatment with AM251 relatively reduced the increased pain threshold, however injection of AM630 failed to antagonize the effect.

Conclusions: This study showed that ferulic acid has a potential in inflammatory pain relief. Cannabinoidergic system is partially involved in ferulic acid induced analgesia by stimulation of CB1 receptors. Because of partial involvement another detailed mechanistic studies should be performed to investigate the acting profile of ferulic acid.

Acknowledgements: This study was supported by a grant of AUBAP-YATP (1805S221-1905S062)

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P164
DEXAMETHASONE-MEDIATED REGULATION OF ERAD MECHANISM AND ITS THERAPEUTIC TARGETING IN HEPG2 HEPATOCELLULAR CARCINOMA CELLS

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Introduction: Hepatocellular carcinoma is one of the most frequently diagnosed liver cancer types in adults (1, 2). Although immunotherapy, radiation, chemotherapy and surgery are the main treatment options for the treatment of hepatocellular carcinoma, acquiring resistance to drug-based therapies limits the effectiveness of treatment (3). Studies have shown that steroid hormones like glucocorticoids may have a regulatory role in liver cancer (4). Glucocorticoids have various uses in medical conditions such as allergies, inflammation, multiple sclerosis and cancer (5). However, their detailed mechanism of action on the physiologically important signal pathways in cancer cells, such as protein quality control mechanisms, has not been fully known yet. Herein, we aimed to investigate the effect of glucocorticoid hormone dexamethasone on the endoplasmic reticulum-associated degradation (ERAD) mechanism in hepatocellular carcinoma cells.

Materials and Methods: Human epithelial-like hepatocellular carcinoma cell line HepG2 was used in the experiments. Cells were propagated in conventional cell culture conditions without antibiotics. To examine the time and dose-dependent effects of dexamethasone on ERAD components, cells were treated with different doses (5-100nM) and time intervals of dexamethasone (0- 24h). The expression mRNA and protein levels of ERAD components were evaluated by qRT-PCR and immunoblotting, respectively. Also, reversal of dexamethasone responses was tested using RU486 antagonist. Additionally, we tested the effects of DsiRNA-mediated targeting of ERAD components on the tumorigenic properties of HepG2 cells, including proliferation, invasion, colony formation and 3D tumor formation.

Results: Our findings revealed that, all tested ERAD components, including Hrd1, gp78, p97/VCP, Ufd1 and Npl4 are modulated by dexamethasone-induced glucorticoid receptor signaling. RU486 efficiently reversed dexamethasone-induced responses. Moreover, DsiRNA-mediated targeting the ERAD components notably reduced the tumorigenic features of HepG2 cells.

Conclusions: Present data suggest that pharmacologically targeting the ERAD components may present a new-era therapeutic approach against hepatocellular carcinoma.

Acknowledgements: This study was supported by Suleyman Demirel University internal funds (TSG-2021-8302 and TAB-2020-8253).

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CANNABIDIOL NEGATIVELY MODULATES ANDROGENIC SIGNALING IN PROSTATE CANCER CELLS

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Introduction: Cannabinoids are broadly-researched compounds obtained from Cannabis species. Although there are more than 120 metabolites isolated from Cannabis species, cannabidiol is one of the most commonly studied compounds among them (1). Its wide-ranging beneficial effects have been demonstrated in both preclinical and clinical studies (2,3). Also, its anti-cancer effect has been demonstrated in many types of cancer, including prostate cancer (4). Although there are different therapeutic approaches in the treatment of prostate cancer, which is the most common cancer in men, the occurrence of castration limits the effectiveness of treatment (5). Thus, there is a need for alternative therapies targeting mechanisms of prostate cancer pathogenesis, such as androgenic signaling. Herein, we aimed to examine the effects of cannabidiol on androgenic signaling in human androgen-responsive prostate cancer cells.

Materials and Methods: Androgen-responsive human prostate adenocarcinoma cell line LNCaP was used in the in vitro experimental studies. Cells were propagated in conventional cell culture conditions. The WST-1 assay was performed to evaluate the effect of cannabidiol on the proliferation of LNCaP cells and determine the half-maximal inhibitory concentration (IC50) of cannabidiol. The effect of cannabidiol on androgen receptor expression and nuclear levels was analyzed by immunoblotting and fractionation assay, respectively. Besides that, the nuclear localization of the androgen receptor was investigated by immunofluorescence microscopy.

Results: In line with our findings, we observed that cannabidiol significantly suppressed the proliferation rate of LNCaP cells. Androgen receptor expression was also notably reduced by cannabidiol treatment in a dose-dependent manner. Moreover, fractionation and immunofluorescence microscopy findings revealed that cannabidiol markedly limited the nuclear level and nuclear translocation of the androgen receptor.

Conclusions: The present data suggest that cannabidiol may be an alternative treatment option in addition to existing therapies for the treatment of prostate cancer by modulating androgenic signaling.

Acknowledgements: This study was supported by Suleyman Demirel University internal funds (TSG-2021-8302 and TAB-2020-8253).

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ALTERATIONS IN APOPTOSIS-ASSOCIATED GENE EXPRESSIONS IN LUNG CANCER CELLS IN THE PRESENCE OF IXAZOMIB AND GIVINOSTAT.

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Introduction: Proteasome inhibitors and histone deacetylase (HDAC) inhibitors hold promise in lung cancer treatment by enhancing cancer cell sensitivity to therapy. Specifically, combining bortezomib, a proteasome inhibitor, with HDAC inhibitors has been shown to sensitize non-small cell lung cancer cells (1). This combined therapy exhibits heightened cytotoxic effects in sensitive cell lines, offering a potential strategy against treatment resistance in lung cancer. Additionally, co-culturing with macrophages has been found to induce alterations in gene expression profiles in lung cancer cell lines (2). Therefore, this study aimed to investigate changes in gene expressions associated with apoptosis in lung cancer cells when exposed to a combination of the proteasome inhibitor ixazomib, the HDAC inhibitor givinostat, and differentiated M1 macrophages.

Materials and Methods: The IC50 values of ixazomib and givinostat on A549 lung cancer cells were determined using the MTT method. A range of concentrations of these drugs (400, 100, 10, and 1 µM) were administered to A549 cells, and their viabilities were assessed after 24 hours. Following exposure to the determined IC50 concentrations for 24 hours, total RNA was isolated from A549 cells treated with ixazomib alone, ixazomib+givinostat, and THP-1 monocyte cells differentiated into M1 macrophages and co-cultured with this combination. Subsequently, RT-PCR experiments were conducted to assess alterations in apoptosis-related genes.

Results: Based on the results of the anti-proliferative effect analysis, the IC50 values for ixazomib and givinostat were determined to be 2.42 µM and 7.32 µM, respectively. According to the RT-PCR results, variations of up to 48.99-fold were observed in the NFKB2, NFKBIA, NFKBIB, RELB, IL-6, IL-8, TP53, PIK3CA, and BCR genes.

Conclusions: Significant alterations were particularly observed in genes involved in apoptosis-related pathways, especially in the presence of M1 macrophages. Additional investigation is warranted to thoroughly explore the heightened inflammatory response observed in lung cancer cells in the presence of these drugs.

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INVESTIGATION OF THE EFFECTS OF PROTOCATECHUIC ACID LOADED NANO-STRUCTURED LIPID CARRIER SYSTEM ON DEPRESSION-LIKE BEHAVIORS IN LPS-INDUCED SYSTEMIC INFLAMMATION IN MICE.

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Introduction: Protocatechuic acid (PCA), also known as 3,4-dihydroxybenzoic acid, is a phenolic compound commonly found in medicinal plants, noted for its potential to inhibit the progression of neurodegenerative diseases. Neuroinflammation, characterized by the release of proinflammatory cytokines (IL-1β, IL-6, and TNF-α) and activation of NF-κB, plays a significant role in these diseases. LPS is used to induce systemic inflammation in animals, imitating depression-like symptoms (1,2). This study aims to investigate the potential of PCA-containing NLC systems in preventing or reducing LPS-induced anxiety and depression-like behaviors.

Materials and Methods: Lipid nanoparticles were prepared using the hot homogenization method, employing Miglyol®812N and Compritol 888 ATO (3). Male BALB/c mice were subjected to hole-board, light/dark box, and tail suspension tests to assess the impact of NLC-PCA on anxiety and depression. NLC-PCA was administered intraperitoneally (75mg/kg) for 7 consecutive days. On the 7th day, 30 minutes post-drug administration, the LPS group received intraperitoneal injections of 0.83 mg/kg LPS. Behavioral experiments (light-dark box, hole board and tail suspension tests) were conducted 1 hour post-injection. Subsequently, mice were euthanized under ketamine/xylazine anesthesia (90-100 mg ketamine and 10 mg xylazine), and total brain tissues were isolated. RT-qPCR was employed to evaluate the expression levels of TLR-4 and NFκB mRNA in brain tissue (4).

Results: NLC-PCA and also NLC-PCA+LPS groups were found significantly effective compared to control or NLC-LPS groups in light-dark box and tail suspension tests. It was shown that TLR4 mRNA expression increased significantly with LPS administration compared to the control (NLC) and NLC+PCA groups. TLR4 mRNA expressions significantly decreased with NLC+PCA administration. Similarly, NFκB mRNA expressions were found to be significantly lower in the NLC+PCA+LPS group compared to the NLC+LPS group.

Conclusions: According to various epidemiological studies, neuroinflammation is considered a major risk factor, and there is reported to be a relationship between systemic inflammation and neuropsychiatric disorders (5). As a result, NLC-PCA administration significantly reduced neuroinflammation, thereby alleviating anxiety-like symptoms triggered by LPS injection in behavioral tests. Our findings suggest the potential of NLC-PCA to improve behaviors and neurochemical changes associated with anxiety-like symptoms.

Acknowledgments: This study was supported by Anadolu University BAP (Project No: 2207S177)

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ANTI-MIGRATION POTENTIAL OF GIVINOSTAT ON HUMAN UMBILICAL VEIN ENDOTHELIAL CELLS.

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Introduction: Angiogenesis is a natural process that involves the proliferation, migration, and differentiation of endothelial cells. Endothelial cell migration, an important step in angiogenesis, plays a crucial role in the development of solid tumors, as it is necessary for their growth and metastasis (1,2). Histone deacetylases (HDACs) are considered important epigenetic markers in cancer, and their overexpression leads to increased metastasis and angiogenesis (3); therefore, givinostat, an HDAC inhibitor drug (4), was used in our study. This study aimed to investigate the antiproliferative and antimigration effects of the histone deacetylase inhibitor givinostat on human umbilical vein endothelial cells (HUVECs).

Materials and Methods: HUVECs represent a widely used source of primary endothelial cells for in vitro studies of angiogenesis (5). In this study, antiproliferative and antimigratory effects were investigated of givinostat on HUVECs. The antiproliferative effects of different concentrations (400, 100, 10, and 1 µM) of givinostat were evaluated by the MTT (3,4,5-dimethylthiazol-2-yl)-2-diphenyltetrazolium bromide) method. Also, the IC50 values of givinostat on cells were calculated using the MS Excel program. Cell migration assays were conducted with a real-time cell analysis system (RTCA DP) by using CIM plates that contain microelectronic sensors connected to the underside of the plate.

Results: We found that givinostat had significant time- and concentration-dependent antiproliferative effects on HUVECs, according to MTT results. The results obtained from the analysis of givinostat indicate that a concentration of 5.35 µM led to a 50 percent reduction in cell viability in HUVECs. In the migration assays, IC25 (2.67 µM) and IC50 (5.35 µM) concentrations of givinostat significantly suppressed migration responses on HUVECs, according to the control group. As a result of our study, givinostat has important antiproliferative and antimigration effects on HUVECs.

Conclusions: These findings imply that givinostat could hold promise as both a preventive measure and a therapeutic intervention for angiogenesis.

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THE EFFECT OF KETOGENIC DIET ON ABSENCE SEIZURES IN GENETIC RAT MODEL OF ABSENCE EPILEPSY.

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Introduction: The ketogenic diet (KD), consisting of sufficient protein, high fat, and low carbohydrate intake, has been shown to be a successful non-pharmacological treatment for drug-resistant epilepsy by producing ketones that serve as an alternative fuel source for the brain, thereby reducing the occurrence of seizures1,2. However, there is limited knowledge on the efficacy of KD in absence epilepsy. Therefore, we aimed to investigate the effects of KD on absence seizures in genetic absence epilepsy rats from Strasbourg (GAERS), which is considered a well-validated animal model of childhood absence epilepsy3.

Materials and Methods: Postnatal (PN) 20-day-old male/female (n=4 and 3; respectively) GAERS rats weighing 25-30 grams were randomly divided into 2 groups and fed either a standard certified carbohydrate diet (SD) consisting of 2.7% fat, 20% protein and %77 carbohydrate or KD consisting of 81.4% fat, 16.2% protein and %2.4 carbohydrate for 40 days. On PN53, rats were implanted with EEG electrodes over the frontoparietal cortex and allowed a week of recovery. On day PN60, a 3h EEG was recorded to evaluate frequency of absence seizures. At PN20 and PN60, body weights were recorded, circulating blood glucose and ketone levels were measured by drawing blood from tail veins. Brain tissues were then isolated and kept at -80°C for molecular analysis.

Results: The KD decreased the number and cumulative duration of absence seizures in male GAERS but not in females at PN60 ($p<0.05$). Additionally, KD reduced body weights and induced ketosis in both genders. Blood glucose levels did not change.

Conclusions: These results suggest that KD exhibits effectiveness in treating absence epilepsy when started at PN20 and gender differences affect this response. Further studies are needed to better understand the effectiveness of KD in treating absence epilepsy.

Acknowledgements: This study was supported by a grant of TUBITAK-2209A University Students Research Projects Support Program. (Project number: 1919B012311506). This project is 5th grade thesis dissertation at Istanbul University Faculty of Pharmacy.

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INVESTIGATION OF THE NEUROPROTECTIVE EFFECT OF METFORMIN AGAINST PENICILLIN-INDUCED NEUROTOXICITY IN SH-SY5Y CELL LINE

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Introduction: Neurodegenerative diseases such as Alzheimer's and Parkinson's cause necrosis of neurons, loss of function, abnormal signal transmission between cells, inflammatory response and insulin dysfunction in the brain. It is estimated that this situation will affect approximately 150 million people globally in 2050 and cause an economic burden of 10 trillion dollars (Temple, 2023). It is thought that metformin, a guanidine-derived antidiabetic agent, may play a neuroprotective role by regulating energy metabolism, oxidative stress, inflammatory response, and preventing neuronal dysfunction and neuron death (Sharma et al., 2021; Du et al., 2022). This study aimed to investigate the neuroprotective effect of metformin against penicillin-induced neurotoxicity in the SH-SY5Y cell line.

Materials and Methods: After seeding SH-SY5Y cells, various concentrations of penicillin and metformin were applied, and at the end of 24 hours, neuronal viability test (MTT) was performed to decide the concentrations of penicillin and metformin for the study. The effect of metformin (10, 20, 40 mM) against penicillin (800 µM)-induced neurotoxicity in SH-SY5Y cells was tested with three different experimental designs (pre-treatment, co-treatment, post-treatment).

Results: Metformin (10, 20, 40 mM) showed a neuroprotective effect in pre-treatment and co-treatment experimental designs, while metformin (40 mM) showed a neuroprotective effect post treatment.

Conclusions: After this stage, we will continue to confirm the neuroprotective effect of metformin in our studies and focus on elucidating the underlying mechanisms.

Acknowledgements: No support was received from any institution/organization for this study.

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PRECLINICAL EVIDENCE OF COMBINED ACTIVITY OF CURCUMIN AND ROSUVASTATIN: EFFECTS ON HEMATOLOGICAL PARAMETERS IN WISTAR RATS WITH DIET-INDUCED HYPERLIPIDEMIA

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Introduction: Lately, the research focus of modern biomedical science is based on a combinational approach that evaluates the synergistic pharmacological activity of natural compounds and synthetic medicine. Investigating the synergistic potential of combining natural with synthetic products can result in an advance in pharmacotherapy, improved pharmacological activity, and reduced side effects (1). This study aimed to investigate the effectiveness of a potentially new synergistic combination of curcumin and rosuvastatin in a model of diet-induced hyperlipidemia in Wistar rats and its impact on various hematological parameters.

Materials and Methods: Sixty Wistar rats were divided into five study groups: Standard control received standard rodent diet; Atherogenic control received atherogenic rodent diet, i.e. modified western-type diet with added cholesterol and chlorate; Curcumin-atherogenic group received atherogenic diet and curcumin (200 mg/kg body weight) by oral gavage; Rosuvastatin- atherogenic group received atherogenic diet and rosuvastatin (10 mg/kg body weight) by oral gavage; Rosuvastatin curcumin- atherogenic group received atherogenic diet and a combination of curcumin and rosuvastatin in mentioned doses and route. Hyperlipidemia was induced by feeding rats with an atherogenic diet for 14 days and feeding further continued for the next 14 days in combination with the treatment (2). On the last day of the study, after overnight fast and free access to water, rats were anesthetized, with an application of ketamine (75 mg/ml) and xylazine (5 mg/ml), and sacrificed. The whole blood samples were collected by cardiac puncture, and the following hematological parameters were determined using a 5DIF Mindray BC-5000 hematological counter: erythrocytes, leukocytes, platelets, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin concentration and mean corpuscular hemoglobin. Also, the leukocyte cells that were analyzed and counted on blood smears are as follows: lymphocytes, monocytes, neutrophil granulocytes, eosinophilic granulocytes, and basophilic granulocytes. Cells of the leukocyte lineage were differentiated and numerical values were expressed as percentages after analyzing 2000 such cells from each experimental animal.

Results: The results demonstrate that induced hyperlipidemia has an anticipated adverse effect on hematological parameters. Moreover, significant alterations in these parameters were observed, providing substantial evidence supporting curcumin and rosuvastatin's beneficial effects.

Conclusions: To date, the combined pharmacological activity of curcumin and rosuvastatin has not been examined, and there is a lack of available information on any potential synergist effects between the two compounds.

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P173
VORTIOXETINE IMPROVED COGNITIVE SYMPTOMS IN MK-801-INDUCED SCHIZOPHRENIA MODEL OF RATS

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Introduction: Schizophrenia is a psychiatric disorder characterized by positive, negative, and cognitive symptoms. (van OS and Kapur, 2009). Current medications are insufficient for adequately treating schizophrenia. While existing treatment approaches can significantly reduce positive symptoms, they are less successful in addressing negative and cognitive symptoms. Vortioxetine antagonizes serotonergic 5-HT3 and 5-HT7 receptors, exhibits agonistic effects on the 5-HT1A receptor, and partial agonist effects on 5-HT1B receptors. This multimodal activity is believed to be responsible for its antidepressant and anxiolytic-like effects, as well as improvements in cognitive functions in animal studies. Due to its multimodal regulatory role in the brain's serotonergic system, vortioxetine is thought to potentially exert an antipsychotic effect on schizophrenia (Bozkurt and Unal, 2023). In our study, we investigated the effects of vortioxetine on the cognitive symptoms of schizophrenia in a rat model induced by MK-801.

Materials and Methods: To establish a schizophrenia model in rats, a single daily dose of MK-801 (0.2 mg/kg, i.p.) was administered for 14 days. Subsequently, treatments of vortioxetine (10 mg/kg) and risperidone (0.3 mg/kg) were administered once daily (i.p.) for 21 days. Y maze test was conducted at the 21th day of treatment to assess the cognitive symptoms in the schizophrenia model in rats.

Results: MK-801 significantly reduced ($p<0.05$) spontaneous alternation compared to the control group. Vortioxetine significantly increased ($p<0.05$) the percentage of alternation reduced by MK-801. However, risperidone, used as a positive control, did not alter the percentage of alternation affected by MK-801.

Conclusions: In the MK-801-induced schizophrenia model, vortioxetine has improved cognitive functions in rats. Moving forward, we will focus on elucidating the underlying mechanisms of this effect of vortioxetine.

Acknowledgements: This study was supported by the Erciyes University Scientific Research Projects Coordination Unit (Proje ID:13707)

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P174
EVALUATION OF MEDICATION REGIMEN COMPLEXITY IN ELDERLY PATIENTS WITH CHRONIC KIDNEY DISEASE

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Introduction: Older adults with chronic kidney disease have highly complex medication regimens (1). This study aims to evaluate the relationship of Medication Regimen Complexity Index (MRCI) score with rehospitalization in elderly chronic kidney disease patients.

Materials and Methods: The study was conducted retrospectively on chronic kidney patients hospitalized in the nephrology service of Suleyman Demirel University Application and Research Hospital. Ethics committee approval was received from Suleyman Demirel University Clinical Research Ethics Committee (Date: 31.10.2023, No: 196). The Turkish validated version of the MRCI was used in the study (2).

Results: 136 patients were included in the study and 63.2% were male. The mean±standard deviation (SD) MRCI score was 23.4 ±13.65. MRCI score was found to be statistically higher in patients with polypharmacy, anticholinergic drug use, diabetes and chronic obstructive pulmonary disease than in those without ($p<0.05$). Serum creatinine values were statistically higher in patients who were rehospitalized within 30 days ($p<0.05$). Also, serum creatinine and MRCI scores were statistically higher in patients rehospitalized within 90 days ($p<0.05$).

Conclusions: According to our study, a high MRCI score was found to be associated with rehospitalization within 90 days. It highlights the importance of medication regimen complexity as a potential target for medical interventions to reduce rehospitalization in elderly chronic kidney disease patients.

Acknowledgements: This study was not supported by any grant.

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P175
PROSPECTIVE EVALUATION OF CLINICAL PHARMACY PRACTICES AMONG PATIENTS IN THE HEMATOLOGY BONE MARROW TRANSPLANTATION UNIT

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Introduction: The presence of clinical pharmacists in the hematopoietic stem cell transplant (HSCT) unit can improve patient safety, optimization of drug therapy, and quality of care (1). The aim of this study is to evaluate clinical pharmacy practices for patients hospitalized in the HSCT unit.

Materials and Methods: In this prospective observational study, which was conducted between June 2023 and January 2024 in the HSCT unit affiliated with Ankara University Hematology Department, the clinical pharmacist attended daily visits and suggested solutions to the drug-related problems (DRPs) they detected, the reasons for the DRPs, the suggestions made and the acceptance of the suggestions. classified its condition according to the v9.1 classification system of the European Pharmaceutical Care Network (PCNE).

Results: In this study, 66 patients were included. A total of 156 DRP were identified. An average of 2.4 DRP was detected per patient. The most common cause of DRP was inappropriate selection of medications (63.2%). The causes of the DRPs are shown in Table 1. The most common reason for the DRPs was inappropriate combination with drugs, herbals or food supplements (56%). The drug group that most commonly causes DRPs was immunosuppressive drugs followed by antifungals and antibacterial drugs. It was determined that there was a significant difference ($p<0.023$) between the number DRPs and the type of transplantation. The average number of DRPs was found to be higher in allogeneic hematopoietic stem cell transplantation (allo-HSCT) patients. A statistically significant difference was found between the number of DRPs and the number of medications ($p<0.001$), presence of comorbidities ($p<0.045$), and length of stay ($p<0.001$). Among 143 suggestions, 135 (94.4%) were accepted. The majority of the DRPs (n=131, 83.9%) were resolved.

Conclusions: It has been revealed that there is a significant correlation between the type of transplantation, length of stay and comorbidity status of the patients and the number of DRP. Most of the intervention suggestions made by the clinical pharmacist towards the solution of DRPs were accepted and most of the problems were solved. In parallel with these findings, it has been observed that a huge portion of drug-related problems are preventable.

Table 1. Causes of drug-related problems

Causes of DRPs	Total number of patients, n=166 (%)	Auto-HSCT, n=73 (%)	Allo-HSCT, n=93 (%)
C1. Drug selection	105 (63.2)	52 (71.2)	53 (57)
C2. Drug form	4 (2.4)	0 (0)	4 (4.3)
C3. Dose selection	6 (3.6)	0 (0)	6 (6.4)
C4. Treatment duration	3 (1.8)	1 (1.4)	2 (2.1)
C6. Drug use process	9 (5.4)	0 (0)	9 (9.7)
C7. Patient related	27 (16.3)	17 (23.2)	10 (10.7)
C8. Patient transfer related	2 (1.2)	1 (1.4)	1 (1.1)
C9. Other	10 (6)	2 (2.7)	8 (8.6)

Allo-HSCT: allogeneic hematopoietic stem cell transplantation Auto-HSCT: Autologous hematopoietic stem cell transplantation

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P176

POSSIBLE EFFECT OF WILMS TUMOR 1 GENE MUTATION ON TACROLIMUS METABOLISM IN ACUTE MYELOID LEUKEMIA: CASE REPORT

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Introduction: Approximately 15% of acute myeloid leukemia (AML) patients have Wilms tumor 1 (WT1) gene mutations and WT1 gene mutations associated with poor clinical outcomes in AML patients (1). There is an interaction between WT1 and the promoter region of the multidrug resistance-1 (MDR1) gene encoding P-glycoprotein (2). We aimed to determine relation between WT1 gene mutation and metabolism of tacrolimus, a P-glycoprotein substrate, in an AML patient.

Materials and Methods: The 32-year-old male patient diagnosed with relapsed refractory AML, who had no comorbidities, received allogeneic peripheral stem cell transplantation with fludarabine, mitoxantron, cytarabine, cyclophosphamide and TBI protocol from match sibling donor. While receiving GVHD prophylaxis with cyclosporine and mycophenolate mofetil, thrombotic microangiopathy developed and cyclosporine was discontinued. Acute liver GVHD was diagnosed and received sirolimus and methylprednisolone, sirolimus was discontinued due to possible pulonary toxicity and tacrolimus was administered. The patient, who was using posaconazole, was administered one-third of the calculated dose due to drug interaction.

Results: Tacrolimus blood concentrations were 59.5 ng/ml detected after 3 doses.

According to the patient's next generation sequencing method, WT1 variant c.1349G>T p.Arg450Leu variant allele frequency (VAF) 5.53% and WT1 variant c.1369C>A p.His457Asn VAF 5.19% were detected.

Tacrolimus is the major substrate of P-glycoprotein and posaconazole is an inhibitor of the Cytochrome P450 3A4 enzyme. It was thought that WT1 gene mutation might reduce tacrolimus metabolism by P-glycoprotein inhibition.

Conclusion: It is possible to say that WT1 gene mutations in AML patients may significantly affect the metabolism of tacrolimus, substrate of P-glycoprotein.

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P177
MEDICATION REGIMEN COMPLEXITY AND ANTICHOLINERGIC DRUG USE IN OLDER CANCER PATIENTS

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Introduction: Elderly cancer patients have polypharmacy and complex medication regimens due to cancer treatment and supportive treatments (1). This study aimed to determine the Medication Regimen Complexity Index (MRCI) score and anticholinergic drug use in elderly cancer patients and to investigate its relationship with rehospitalization.

Materials and Methods: This study was conducted retrospectively on elderly cancer patients over the age of 65 who were hospitalized in the oncology service of Suleyman Demirel University Application and Research Hospital. Ethics committee permission was obtained from Suleyman Demirel University Clinical Research Ethics Committee (Date: 05.12.2023, No:254). MRCI Turkish version was used (2). Anticholinergic drug use was defined as anticholinergic cognitive burden scale (ACBS) score ≥1 (3).

Results: 137 patients were included in the study. 37.2% of patients were female and the median age was 70 years (IQR, 67-76). Anticholinergic drug use (ACBS ≥ 1) was present in 25.5% of patients. MRCI scores were statistically higher in those who were rehospitalized within 30 days, in the presence of polypharmacy, and in those using anticholinergic drugs ($p<0.05$). A statistical relationship was found between rehospitalization within 30 days and high MRCI score only ($p<0.05$). No statistical association was found between the variables and rehospitalization within 90 days ($p>0.05$).

Conclusions: MRCI could be an important determinant of rehospitalization in cancer patients and further studies are needed on this subject.

Acknowledgements: This study was not supported by any grant.

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P178
EVALUATION OF DRUG-RELATED PROBLEMS IN A LIVER TRANSPLANTATION SERVICE

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Introduction: Liver transplantation (LT) has emerged as a lifesaving treatment for patients suffering from end-stage liver disease and acute liver failure. However, long-term care for LT recipients involves adherence to complex therapeutic regimens which can lead to the occurence of drug-related problems (DRP) (1). DRPs are often viewed as safety issues, contributing to increased healthcare costs, hospital readmissions and mortality, and reduced quality of life (2). Although several DRP classification systems exist in the literature, the Pharmaceutical Care Network Europe (PCNE) system stands out for its detailed approach that closely aligns with the nature and the causes of DRPs (3). We aimed to determine and classify the DRPs in the liver transplantation service of a university hospital using the PCNE DRP classification system.

Method: The study was conducted prospectively over a period of six months, from May 5, 2023, to October 10, 2023. Patients who were hospitalized in the liver transplantation service and were receiving at least one medication were included in the study. Demographic and clinic data of patients, as well as DRPs were recorded. DRPs in their medical therapy were evaluated using PCNE v.9 version. Statistical analyses of the obtained data were performed using the IBM SPSS version 23.

Results: A total of 33 patients were evaluated. The median value of age was 56 (IQR: 1-75) and 66.7% (n=22) of the patients were male. The most common reason for admission were cirrhosis (27.3%), hepatitis B infection (18.2%) and hepatacellular carcinom (15.2%). A total of 111 DRPs were detected with an average of 3.4 DRPs per patient. The most commonly identified DRPs were adverse drug reaction (possibly) occuring (52.3%), effect of drug treatment not optimal (29%), and untreatment symptoms or indication (21%). The most common reasons for DRPs were, respectively, drug use process (40.3%), drug selection (27.5%) and dose selection (20.6%). The interventions were, respectively, at prescriber level (63.3%) and at drug level (31.2%). The most common interventions at drug level to resolve DRPs were dose changes (15.6%), discontinuation of the medication (8.3%) and drug started (6.2%). 86.6% of the interventions were accepted, and 78.4% of the DRPs were completely resolved.

Conclusion: This study has demonstrated the effectiveness of clinical pharmacists in preventing DRPs arising as a result of immunosuppressive therapy in patients undergoing liver transplantation. The involvement of clinical pharmacists in the multidisciplinary team for the detection and prevention of drug-related problems will play a crucial role in ensuring treatment safety and effectiveness for patients.

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P179
THE RADICAL SCAVENGING AND CYCLOOXYGENASES INHIBITORY EFFECTS OF ALCHEMILLA DAGHESTANICA JUZ

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Introduction: The genus Alchemilla L. is represented by more than 1000 species worldwide and 74 species in Türkiye, 35 of which are endemic (1,2). The genus Alchemilla is known as "Lady's mantle" in Europe and "aslan pençesi" in Türkiye and is used internally for gynecological and inflammatory diseases; and externally for dermatological diseases such as wounds, eczema, etc. (3). Various studies on Alchemilla species have shown that the genus is rich in tannins, flavonoids, proanthocyanidins, triterpenes and phenolic acids (4). In addition, various biological activity studies such as antimicrobial, antiinflammatory (4), antioxidant (3), neuroprotective (5) effects of various extracts and pure compounds isolated from plants are found. In this study, the biological activities of methanol extracts prepared from the aerial and root parts of Alchemilla daghestanica Juz growing in Türkiye (ISTE 118080) were investigated.

Materials and Methods: The roots and aerial parts of A. daghestanica in flowering stage were collected, dried, milled and extracted. Each part was macerated with methanol:water (80:20) at 24°C for 8 h. The process was repeated 3 times, and the solvent was removed (5). The extracts were named ADR (A. daghestanica roots) and ADH (A. daghestanica aerial parts). The total phenolic and flavonoid content, 2,2-diphenyl-1-picrylhydrazyl radical scavenging, and cyclooxygenase 1/2 (COX1/2) inhibitory effects of the extracts were investigated using spectrophotometric assays.

Results: The results of total phenolic content showed that ADR and ADH were 144.32 ± 7.46 and 6.37 ± 0.95 mg GAE/g dry weight, respectively, and the total flavonoid content of ADH was calculated as 156.18 ± 2.82 mg QE/g dry weight. In the DPPH radical scavenging studies, both extracts exhibited radical scavenging activity depending on the concentration. ADR and ADH at 50 µg/mL were 68.70 ± 1.58% and 40.66 ± 5.96%, respectively. The IC50 values of ADR were evaluated to be 11.25 µg/mL for COX 1 and 37.04 µg/mL for COX 2.

Conclusions: For the first time, a biological activity study was carried out on this species A. daghestanica and the studies show that the species is promising as a potent antiinflammatory agent and should be further investigated.

Acknowledgements: This study was supported by The Scientific Research Projects of Karadeniz Technical University (Project number: THD-2023-10891).

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P180
INVESTIGATION OF THE EFFECT OF ARONIA (ARONIA MELANOCARPA) ON RATS EXPOSED TO RADIATION

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Introduction: In modern life, it is almost impossible to completely avoid radiation. Radiation from both natural sources and man-made sources constantly creates adverse effects on humans and other organisms. After oxidative damage occurs in the organism, the negative effects of free radicals can be prevented by antioxidants taken with food. As a result of studies on Aronia (Aronia Melanocarpa), it has been observed that it has a higher anthocyanin amount and antioxidant capacity compared to other berries [1]. According to the results of animal experiments; It has been found that aronia anthocyanins reduce lipid peroxidation and increase the activity of enzymes involved in the antioxidant defense system [2]. After radiotherapy, the reduction of symptoms due to liver damage occurring in the acute or chronic period is very important for the patient's quality of life. In this study, it was aimed to investigate the protective effect of aronia plant, which has an antioxidant effect, against liver damage caused by radiation.

Materials and Methods: In this study, 24 male Wistar albino rats were used. Rats were divided into 4 groups. Tumor necrosis factor alpha, interleukin 1 beta, 8-hydroxy-2-deoxyguanosine, malondialdehyde levels, superoxide dismutase and catalase enzyme activities were measured to determine inflammation, DNA damage and oxidative stress in the groups treated with aronia and radiation.

Results: When oxidative stress parameters and antioxidant levels were examined, the MDA level in the group receiving both aronia and radiation was statistically significantly lower than in the group receiving radiation alone. SOD and CAT levels increased, but this increase was not statistically significant. It was observed that the application of aronia reduced the levels of inflammation markers TNF-α and IL-1β, but this difference was not statistically significant. To measure oxidative DNA damage, 8-OhdG levels were examined. It was observed that aronia administered with radiation reduced 8-OhdG levels, and this difference was statistically significant.

Conclusions: According to these results, it is thought that aronia can be used as a protector against the side effects of radiotherapy.

Acknowledgements: This study was supported by Mersin University Scientific Research Projects Coordination Unit (Project Number: 2023-1-TP2-4868)

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P181
DETERMINING THE ASSOCIATION BETWEEN HOMOCYSTEINE AND PTX3 LEVELS IN CORONARY ARTERY DISEASE

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Introduction: Coronary artery disease (CAD) is the leading global cause of mortality. CAD is characterized by the narrowing and obstruction of coronary arteries due to atherosclerosis, which begins in fetal life, progresses slowly during childhood and adolescence, and accelerates in adulthood [1]. Many risk factors have been identified that initiate or cause atherosclerosis to progress. Among the etiological factors, hyperlipidemia, hypertension, diabetes and smoking are the leading ones [2]. At the same time, hyperhomocysteinemia and pentraxin 3 (PTX3), an indicator of inflammation, are among the new risk factors for atherosclerosis. It is thought that the atherogenic property of hyperhomocysteine is due to damage to the endothelium [3]. PTX3 is produced by different cell types potentially involved in atherosclerosis, especially endothelial cells (EC), smooth muscle cells, and macrophages. Staining of advanced atherosclerotic lesions in humans also showed strong expression of PTX3 by smooth muscle cells, primarily macrophages and EC [4]. This study aims to investigate the association between Homocysteine and PTX3 levels and CAD.

Materials and Methods: The study included individuals who had been diagnosed with coronary artery disease (n=80) following coronary angiography at Mersin University Faculty of Medicine Hospital Cardiology outpatient clinic, as well as individuals (n=81) considered healthy after coronary angiography. In the study, Human HCY (Homocysteine) and human PTX3 ELISA Kit (Fine Test, Wuhan, China) were used to measure homocysteine and PTX3 levels. Mann Whitney U test was used to compare patient and control groups. The significance level of the tests for all analyzes was determined as $p<0.05$.

Results: When PTX3 levels were compared between the control and patient groups, the difference was found to be statistically significant ($p<0.05$). However, it was determined that the homocysteine levels of the control group participating in our study were significantly higher than the patient group. This situation constitutes an exception to the general trend in the relationship between homocysteine levels and vascular risk in our study.

Conclusions: These findings indicate the potential significance of homocysteine and PTX3 levels in assessing coronary artery disease risk and monitoring patients. However, these results need to be confirmed and strengthened through larger and more comprehensive studies.

Acknowledgements: This study was supported by Mersin University Scientific Research Projects Coordination Unit (Project Number: 2021-1-TP3-4171).

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P182
SYNTHESIZING NEW CARBAZOLES VIA DIELS-ALDER REACTION: EVALUATION AS CHEMOTHERAPEUTIC AGENTS FOR BRAIN CANCER

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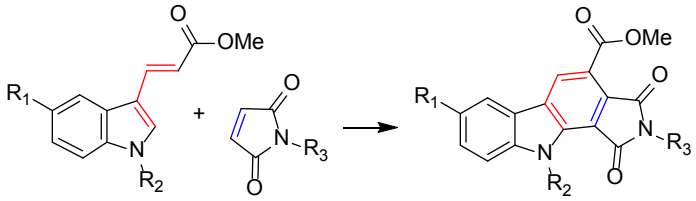
Introduction: Brain tumours lend major barriers in the field of oncology, requiring the investigation of novel therapeutic approaches. In this study, we synthesized 12 novel carbazole compounds that were produced via the Diels-Alder reaction. Among more conventional alternatives, carbazole compounds have demonstrated extremely promising anticancer activities both in vitro and in vivo.1. The successful use of carbazole-based chemicals in medications like ellipticine, elliptinium acetate (Celiptium®) is one example of how these compounds have shown promise in cancer therapy.2 The importance of investigating carbazole-based drugs in search of efficient therapies for diverse brain malignancies is highlighted by this study.



Materials and Methods: To assess their effectiveness against glioblastoma and neuroblastoma, the cell lines U-87 MG and SH-SY5Y were used. These cell lines were studied at 5, 10, 20, 40, and 80 µM concentrations during a 24-hour incubation period. Furthermore, the effects on healthy L929 cell line were examined under the same conditions to assess selectivity.

Results: MTT assays were conducted to assess cell viability for each drug. Different drugs exhibited distinct IC50 values; for instance, compound 14P demonstrated an IC50 of 79 µM with U-87 MG cell line. The findings indicate our ability to evaluate the cytotoxic effects of compounds on cancer cell lines and how their therapeutic potential varies based on their functional groups.

Conclusions: Early results show that our synthesized carbazole derivatives have moderate to good cytotoxic action against neuroblastoma and glioblastoma cells, suggesting that they may be useful as therapeutic agents for brain cancers.

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P183
CELL VIABILITY AND MIGRATION EFFECTS OF AURELIA AURITA JELLYFISH POLAR EXTRACTS ON HUMAN SKIN FIBROBLASTS

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Introduction: Marine life has been investigated as a new potential source of bioactive compounds. Jellyfish have been found to show diverse advantageous effects such as antibacterial, antifungal, antioxidative and wound healing due to their rich content [1]. Wound healing is a critical process to maintain the barrier of skin and preserve other skin functions [2]. One of the most common jellyfish species in the Türkiye, Aurelia aurita, shares a similar content with other jellyfish and might be beneficial in the wound healing process [3,4]. Therefore, we aimed to investigate the effects of A.aurita extracts on human skin fibroblast cell line by examining cell viability and migration rates.

Materials and Methods: A.aurita extracts were prepared using ethanol and water. CCD-1079Sk cells were used for cytotoxicity and migration assays. After treatment with A.aurita extracts for 24 and 48h, absorbance was recorded and the cytotoxicity was expressed as the concentration of the sample that inhibited 50% of cell growth. For migration, a scratch on the surface of the plate was made. After treatment with extracts, photos of the scratch were taken at different time points. The gap size was analyzed and the rate of cell migration was calculated. All statistical analysis was performed using GraphPad Prism 10. $p<0.05$ was considered statistically significant.

Results: Cell viability test (MTT) showed that A.aurita extract treatments promoted proliferation rates, especially after 24h. IC50 values of the ethanol extracts were 13.3±1.2µg/mL for 24h and 141.1±1.2µg/mL for 48h. Further, we investigated whether extracts could induce changes in cell migration rates using scratch assay. Our data indicated that A.aurita extract treatment increased cell migration by 2.5 times after 31h. Wounds showed a significant reduction in treatment groups ($p=0.01$).

Conclusions: Our data suggests a correlation between treatment with A.aurita extracts and human skin fibroblast migration, potentially offering an opportunity to be beneficial in wound healing. This study may serve as a basis for the possible advancement of these marine compounds into potent wound care medication. Nevertheless, additional research is required to assess toxicity and safety profiles thoroughly.

Acknowledgements: This study was funded by the Scientific and Technological Research Council of Turkey (TUBITAK) BIDEB 2209a Grant No 1919B012317747.

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P184
EFFECTS OF AMITRIPTYLINE ON CELL VIABILITY AND APOPTOSIS IN ACUTE MYELOID LEUKEMIA CELL LINE

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Introduction: Acute myeloid leukemia (AML) is a clonal hematopoietic stem cell malignancy characterized by the accumulation of immature progenitor cells, leading to suppression of hematopoiesis (1). Amitriptyline is an FDA-approved medication used to treat depression in adults (2). In our study, the effects of amitriptyline on cell viability, apoptosis and mitochondrial mass were determined in HL60 cell line.

Materials and Methods: The effect of amitriptyline on the proliferation of HL60 cells was determined by MTT test, its effect on apoptosis was determined by flow cytometry and caspase assay, and its effect on mitochondrial mass was determined by fluorometric analysis as a result of staining with acridine orange.

Results: Amitriptyline significantly reduced the viability of HL60 cell line in the concentration range of 20-100 µM at 24 hours, 0.1-100 µM at 48 hours, and 0.05-100 µM at 72 hours. Amitriptyline significantly increased caspase 3 activity at 60 µM concentration. Also it significantly increased early apoptosis at 40 µM and 60 µM concentration, increased late apoptosis at 40 µM and 60 µM and increased necrosis at 40 µM and 60 µM after 72 hours of incubation. In addition, when the effects of amitriptyline on mitochondrial mass were examined, it significantly reduce mitochondrial mass at 60 µM concentration after 72 hours of incubation.

Conclusions: This is a study examining the cytotoxic and apoptotic effects of amitriptyline on HL60 leukemia cells. In future studies, the effects of amitriptyline on genes and proteins in the pathways involved in apoptosis and mitochondrial proteins can be clarified by examining them in more detail.

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P185
ICRT14 INDUCES APOPTOSIS THROUGH MLH1 OVEREXPRESSION IN AML CELL LINE

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Introduction: Acute myeloid leukemia (AML) is a heterogeneous and aggressive clonal disease of haematopoietic stem cells (HSPC) in the bone marrow. The Wnt/β-catenin pathway is an evolutionary conserved signal transduction cascade with significant roles in normal embryonic development and disease. Recent studies have represented that dysregulated Wnt/β-catenin signalling in AML which can be broadly divided into cell intrinsic and extrinsic influences. Several studies have shown that β-catenin protein is overexpressed generally in AML blasts or cell lines versus levels in normal HSC. It is also reported that Mismatch repair (MMR) process is clearly linked to cell cycle checkpoint activation and cell death. It appears that DNA damage recognized by the MMR proteins triggers an unsuccessful repair process, which leads to the MMR-dependent cell cycle arrest. In this study, we analyzed the apoptotic effects of iCRT14 which is an inhibitor of β-catenin responsive transcription in AML cell line (HL60).

Materials and Methods: To define the apoptotic effects of iCRT14 in HL60 cells, we treated the cells with 25μM and 50μM iCRT14 for 48h. Later, we performed flow cytometry analysis for annexinV and casepe3/7 activity. Moreover, we evaluated beta-catenin and MLH1 mRNA expression levels in iCRT14 treated cells compared to the control cells.

Results: According to our annexin V and Caspase 3/7 assays, iCRT14 induced apoptosis in all treated cells compared to the control group significantly and time dependently. Furthermore, β-catenin expression level decreased slightly whereas, MLH1 mRNA gene expression levels enhanced significantly in treated cells compared to the control group.

Conclusions: This study reported that, β-catenin downregulation and MLH1 upregulation are involved in the apoptosis induction in iCRT14 treated HL60 cells compared to the untreated cells.

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P186
PREPARATION OF W/O MICROEMULSION AS A TRANSDERMAL DELIVERY SYSTEM FOR NALTREXONE HYDROCHLORIDE: PHYSICOCHEMICAL CHARACTERIZATION

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Introduction: Naltrexone HCl, an active ingredient used to counteract the effects of opioids through its interaction with opioid receptors. However, the main aim of our study is to develop highly stable microemulsion formulations that increase the dermal absorption of naltrexone HCl, given its high water solubility, and to reveal their in vitro characteristics.

Materials and Methods: Phase diagrams were constructed through titration of various ratios of surfactant/co-surfactant (S/CoS) mixtures with distilled water at 25 ± 2°C. Different microemulsion regions were obtained from distinct ratios. The S/CoS weight ratios were determined as 1:1, 1:2, 1:3, 2:1, and 3:1. Microemulsions (MEs) were prepared using linseed oil as oil phase, Span 60 as surfactants, polyethylene glycol 400 as co-surfactant, and distilled water as the aqueous phase. For drug loaded MEs, naltrexon hydrochloride solution (mg/ml) was slowly incorporated into the oil phase under magnetic stirring at 1 mg/mL (w/v) and mixed vigorously. Afterwards, the obtained emulsion system was ensured to be uniform in droplet size with microwave effect. Stability studies and physicochemical evaluations were made on the prepared MEs.

Results: In the phase diagrams determined by working at different S/CoS ratios, it was observed that the largest microemulsion area was obtained at a ratio of 1:3. Additionally, the average droplet size of MEs was determined to be 200 nm. However, pH, zeta potential, viscosity and conductivity values of ME formulations were determined to be suitable for W/O type ME formulations. However, MEs were determined to be stable for three months at various temperature conditions (4°C, 25°C, and 37°C) to control for signs of phase separation, aggregation, or precipitation.

Conclusions: Apart from its known therapeutic effect, it has been concluded that w/o type MEs can be prepared in order to increase the transdermal absorption of naltrexone HCl, which is intended to be used in the treatment of Cutaneous Leishmania. The next step of the study will be to determine its anti-Leishmanial activity.

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P187

3D-PRINTED STRONTIUM RANELATE LOADED SILK FIBROIN/ALGINATE-BASED SCAFFOLDS FOR ALVEOLAR BONE REGENERATION

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Introduction: 3D printing technology has been an extremely essential strategy for producing tissue scaffolds that can be used to replace damaged tissues (1). Strontium ranelate (SR) is a drug improves in bone healing in fractures and in bone defects. Silk fibroin(SF) and alginate are biocompatible, and biodegradable natural-origin polymers(2). The aim of this study is to develop and in vitro evaluate strontium ranelate loaded SF/alginate-based scaffold with and without the addition of hydroxyapatite for alveolar bone regeneration.

Materials and Methods: Silk fibroin was produced from silkworm cocoons. Silk fibroin and sodium alginate-based SR loaded ink formulations were developed and optimized with the viscosity, surface tension and printability measurements. The formulations were printed in grid structure layer by layer with the extrusion-based 3D printer. The printed formulations were crosslinked with the 5% CaCl2 solution and lyophilized to obtain a porous structure. The scaffolds were evaluated for morphological and structural characterization using scanning electron microscopy(SEM), differential scanning calorimetry(DSC) and fourier transformed infrared spectroscopy(FTIR). In-vitro release studies of scaffolds were carried out using Franz type diffusion cells for 10 days.

Results: The inks were found printable and the viscosity values of the inks were found to be approximately 50 Pa.S and the surface tension values were approximately 37 mN/m. No peak of SR was seen in the DSC and FTIR analysis of scaffolds since the amount of SR in the scaffolds was low. In morphological analysis, it was observed that the scaffolds had a porous structure. Controlled release of SR from the scaffolds was obtained for 10 days, approximately 75% SR release was observed in the first 24 hours, 100% release was achieved in 10 days.

Conclusions: It was concluded that the silk fibroin/alginate-based SR loaded scaffolds were successfully printed with the 3D printing technology and in vitro characterization studies showed that the scaffolds have a potential for alveolar bone regeneration.

Acknowledgement: This study was supported by Gazi University Scientific Research Projects Coordination Office with guided project grant number TSG-2022-7922.

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P188
DESIGN AND EVALUATION OF OPHTHALMIC DELIVERY SYSTEM FORMING IN-SITU GEL CONTAINING BERBERINE

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Introduction: This study focuses on developing a novel in-situ gelling formulation for improving patient compliance with eye treatment. This gel form aims to extend eye contact time, thereby enhancing the absorption and bioavailability of the active ingredient.

Materials and Methods: Berberine, K-carrageenan Pluronic F-127 and Chitosan were purchased from Sigma.

Formulations were prepared using Pluronic F-127, chitosan, and k-carrageenan solutions. Formulations were prepared using the cold method (1). These formulations were assessed for clarity, pH, gelation temperature. Berberine was added to the chosen formulation.

Results: Pluronic F-127 solutions (15-20% w/v) were tested for gelation temperature. Pluronic F-127 solutions were combined with chitosan and examined for pH and gelation temperatures. K-carrageenan was added to the gelled formulations at 30-35°C in order to the optimization of formulations.

Table 1. Formulation parameters and properties

Formulation Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13
Pluronic F127 (%w/v)	20	18	17	16	15	18	18	17	17	17	16	15	15
Chitosan (%w/v) ml	-	-	-	-	-	%1.5 1 ml	%1.5 0.5 ml	%1.5 1 ml	%1.5 0.5 ml	%1.5 0.25 ml	%1.5 0.5 ml	%1.5 0.5 ml	% 0.1 0.5 ml
K-carrageenan (%w/v) ml	-	-	-	-	-	-	-	-	-	-	-	-	% 0.5 2 ml
pH ± SD	6.91 ±0.02	6.94 ±0.03	6.90 ±0.02	6.90 ±0.03	6.89 ±0.02	4.52 ±0.01	4.76 ±0.02	4.95 ±0.03	5.12 ±0.03	5.38 ±0.03	5.27 ±0.03	5.22 ±0.01	5.51 ±0.01
Gelling Temperature ± SD	26°C ±2	27°C ±1.2	28°C ±1	29°C ±1.5	32°C ±2	30°C ±1	28°C ±2	39°C ±1.5	34°C ±1	31°C ±0.5	39°C ±1	40°C ±1	32°C ±1

All formulations were completed to 10 ml with buffer solutions which is pH 7.4

Conclusions: The study identified an optimal formulation for the in-situ gelling system. The formulation consists of 15% Pluronic F127, 0.005% chitosan, and 0.1% , with a pH of 5.5 and a gelation temperature of 32°C. Berberine was incorporated at a concentration of 26%, with corresponding pH and gelation temperature were measured.

Acknowledgements: This study was supported by a grant of TUBITAK (2209-A)

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P189
DEVELOPMENT AND VALIDATION OF STABILITY INDICATING ANALYTICAL METHODS FOR RIBOCICLIB, A DRUG FOR THE TREATMENT OF CERTAIN TYPES OF BREAST CANCER

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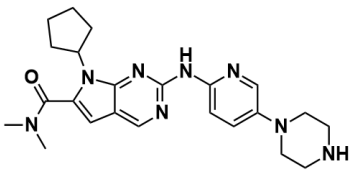
Introduction: Ribociclib is a CDK4/6 inhibitor used for the treatment of hormone receptor (HR)-positive and human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer, which is the most frequently reported cancer among women worldwide (1,2). The aim of this study was to develop stability-indicating analytical methods to investigate the degradation of ribociclib and its salts under stress and stability testing conditions.



Ribociclib
7-Cyclopentyl-*N*,*N*-dimethyl-2-((5-(piperazin-1-yl)pyridin-2-yl)amino)-7*H*-pyrrolo[2,3-*d*]pyrimidine-6-carboxamide
$C_{23}H_{30}N_8O$; MW: 434,54

Materials and Methods: The reference standards were synthesized and characterized by spectroscopic methods (NMR, MS, IR, etc.). A Shimadzu 20A HPLC equipped with an SPD-2A UV detector (Shimadzu Co., Japan) was employed. The Svea Gold C18 column (250 mm × 4.6 mm, 5 µm) was utilized at 30 °C with a 10 µL injection volume at a detection wavelength of 240 nm and a sample temperature of 25 °C. In both the assay and related substances (45 min) methods, gradient elution was employed using a potassium phosphate buffer as the mobile phase A and a mixture of acetonitrile and methanol (50:50, v/v) as the mobile phase B.

Results: The stability-indicating assay and related substances HPLC methods were developed and validated in accordance with ICH Q2 and found to be specific, selective, sensitive, linear, precise, accurate, and robust. The HPLC methods were used during stress testing and stability studies of ribociclib and its salts in accordance with ICH Q1A/Q1B.

Conclusions: The results of the thermal stress testing studies (105 °C, 10 d) demonstrated that ribociclib hydrochloride (99.6%) exhibited the highest stability, followed by ribociclib (99.2%), ribociclib maleate (98.5%), ribociclib succinate (93.4%), ribociclib L-tartrate (85.6%), ribociclib fumarate (84.8%), and ribociclib S-malate (23%).

Acknowledgements: This study was supported by DEVA Holding A.S. (Türkiye) and TUBITAK (BIDEB-2244, Project No: 119C063, Ph.D. scholarship for V. Gok).

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DEVELOPMENT AND VALIDATION OF STABILITY INDICATING ANALYTICAL METHODS FOR INDACATEROL MALEATE

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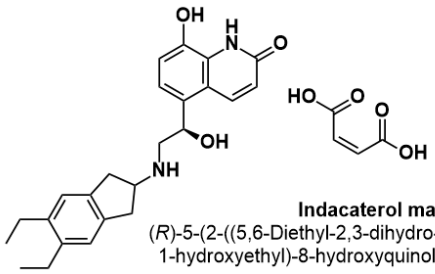
Introduction: Indacaterol is an ultra-long-acting, rapid-onset β2-adrenoceptor agonist utilized for the treatment of chronic obstructive pulmonary disease (COPD) (1-2). The objective of this study is to develop and validate novel stability-indicating analytical methods for the analysis of indacaterol maleate and its potential organic impurities.



Indacaterol maleate
(*R*)-5-(2-((5,6-Diethyl-2,3-dihydro-1*H*-inden-2-yl)amino)-1-hydroxyethyl)-8-hydroxyquinolin-2(1*H*)-one maleate

Materials and Methods: Chromatographic separation of indacaterol and its potential impurities (imp. A-H) was performed on a Shimadzu 20A HPLC system equipped with an SPD-2A UV detector and an LC solution data handling system (Shimadzu Co., Japan). Waters Symmetry (250 mm × 4.6 mm, 5 µm) column was used at 30 °C. Sample temperature, injection volume, and detection wavelength were 25 °C, 10 µL, and 210 nm. The gradient elution was employed. 0.1% o-phosphoric acid (85%) solution was used as diluent and mobile phase A while mobile phase B was a mixture of acetonitrile and mobile phase A (30:70, v/v).

Results: The stability-indicating assay (35 min) and related substances (55 min) HPLC methods for the quantification of indacaterol and its eight potential impurities (precursors, intermediates, regioisomers, dimers, degradation products, etc.) were developed and validated according to ICH Q2. These specific, selective, sensitive, linear, precise, accurate, and robust HPLC methods were used during stress testing and stability studies of indacaterol maleate according to ICH Q1A/Q1B.

Conclusions: Indacaterol maleate is insensitive to elevated temperature (105 °C, 21 d), day light (26 d) and UV radiation (26 d). It showed slight degradation under oxidative conditions (30% H2O2, 45 °C, 7 h, 0.42% imp.), and significant degradation under neutral (water, 100 °C, 18 h, 4.35% imp.), acidic (5 M HCl, 45 °C, 7 h, 3.06% imp.), and alkaline (5 M NaOH, 25 °C, 19 h, 6.97% imp.) hydrolysis conditions. None of the degradation products formed under stress testing conditions was observed during standard accelerated and long-term stability testing of indacaterol maleate.

Acknowledgements: This study was supported by DEVA Holding A.S., Tekirdağ/Türkiye.

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P191
THE EFFECT OF PROTOCATECHUIC ACID IN CAPSAICIN-INDUCED INFLAMMATORY PAIN AND POSSIBLE MECHANISMS

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Introduction: Pain is an unpleasant sensory and emotional experience connected with tissue damage and inflammation (1). Although there are a lot of painkillers, serious complications make the herbal medicines more common around the world as alternative treatment (2). Protocatechuic acid is a natural bioactive compounds that has shown promising anti-inflammatory and analgesic activity (3). In this study, it is aimed to investigate the analgesic effect of protocatechuic acid in capsaicin-induced inflammatory pain mode, and the controbution of opioidergic and a2-adrenergic systems in the effect of protocatechuic acid.

Materials and Methods: The inflammatory pain was induced by i.pl. injection of 20 µg capsaicin (in a volume of 20 µL) in adult female Sprague-Dawley rats. Protocathechuic acid at the doses of 150, 300 and 600 µg were injected, i.pl. (in a volume of 30 µL) 15 min before the capsaicin injection. Non-specific opioid antagonist naloxone (5 mg/kg, i.p.), a2-adrenoceptor antagonist yohimbine (1 mg/kg, i.p.) were used in the mechanistic studied. All pain thresholds were measured with an electronic von Frey device at 0-180 min time interval.

Results: Significant increases in threshold value and reduction in sensitivity to pain was noticed in the protocatechuic acid-treated animals at all doses and time points tested. Yohimbine and naloxone significantly (*p<0,05) antagonized the analgesic effect of 300 µg protocatechuic acid.

Conclusions: As a result, the preclinical data indicates that protocatechuic acid is a potential agent that might be used for inflammatory pain relief. Stimulation of opioidergic and a2-adrenergic systems were involved in the effect of protocatechuic acid, however it seems not to be primary mechanisms of the effect of protocatechuic acid. More studies are required to understand how protocatechuic acid organizes the interactions of pain modulatory systems.

Acknowledgements: This study was supported by a grant of AUBAP-YATP (1805S221-1905S062). This study was approved by (No: 2018-34, No: 2019-13, No: 2019-23) by the Local Ethics Committee of Anadolu University, Eskisehir, Turkey.

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SYNTHESIS OF SOME CHROMONE-2-CARBOXAMIDES AND EVALUATION OF THEIR ANTIMICROBIAL ACTIVITIES

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Introduction: Antimicrobials are life-saving molecules that have helped eliminate different types of infections over the last 100 years and still have an important role in medical practices. Broad-spectrum antibiotics are important in spite of the fact that they can cause many side effects and antimicrobial resistance (1). New molecules are synthesized with efficient and strategic pharmacophore modeling, possessing a wide range of biological activities. The chromone ring is a prominent heterocyclic substructure found in natural and pharmacologically active compounds (2,3). Since there is a need to develop new antimicrobials, it is aimed to synthesize chromone carboxamide derivatives by using the pharmacophore modeling and test their antimicrobial activity.

Materials and Methods: Starting from chromone-2-carboxylic acid, the acyl chloride was first prepared. Afterwards, by reacting with different amine derivatives, chromone-2-carboxamide derivatives were synthesized. The structural determination of the synthesized compounds was carried out using 1H-NMR, 13C-NMR, and mass spectral data. The antimicrobial activities of the synthesized compounds were determined by the minimum inhibitory concentration (MIC) test using the microdilution method (4).

Results: In this study, the synthesis, structural elucidation, and antimicrobial activity evaluation of some compounds with various pharmacophores attached to the C-2 position of the chromone ring were carried out.

Conclusions: The studies and evaluations conducted on the target compounds that are bearing carboxamide derivatives on the second position of the chromone ring, have been promising in terms of antimicrobial activity. Considering that antimicrobial resistance continues to be an important problem today, this study will shed light for the design of more active antimicrobial compounds.

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DEVELOPMENT AND EVALUATION OF NANOFIBERS AS A POTENTIAL BUCCAL DELIVERY SYSTEM FOR ORAL ULCER

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Introduction: Poly(meth)acrylates (Eudragit®) are mucoadhesive and synthetic polymers(1). PVP(Polyvinylpyrrolidone) is a water-soluble and biodegradable polymer(2). Hydrocortisone is used for the treatment of oral ulcers with low solubility in water(3). The aim of this study is to develop electrospun nanofiber with PVP and different types of Eudragit for local treatment of oral ulcers.

Materials and Methods: Different concentrations of Eudragit derivatives(E100, S100 and L 100-55) and PVP (M.W. 40,000) were used in nanofiber formulations. Ethanol: N,N-Dimethylformamide (DMF) (7:3) was used as a solvent system in electrospinning process. Contents and codes of nanofibers are given in the Table 1. Polymer solutions were characterized in terms of surface tension, viscosity(at 20 rpm), and conductivity. The contact angle, mechanical and mucoadhesive properties of the nanofiber formulations were characterized. In-vitro permeability studies of nanofibers were carried out using Franz type diffusion cells(n=3) and were carried out for 24 h using pH:6.8 phosphate buffer as a diffusion medium.

Table 1. Content and codes of nanofiber formulations

Formulation Code	Eudragit S100 (%w/v)	Eudragit L100-55 (%w/v)	Eudragit E100 (%w/v)	PVP (%w/v)	Hydrocortisone (HC) (%w/v)
ES	10	-	-	5	1
EL	-	10	-	5	1
EE	-	-	30	10	1

Results: The characterization results of polymer solutions and nanofiber formulations are given in Table 2. Since the solvent system is the same in polymer solutions, conductivity and surface tension values were found to be similar. The highest tensile strength and elongation at break values were found in the EL formulation while highest mucoadhesion was found in EE formulation. Contact angles values were found high due to hydrophobic nature of polymers.

The Formulations ES, EL and EE released 94,486%, 91,307% and 67,71% of the drug within 8 h, respectively. The EL nanofiber formulation showed optimal mechanical properties and drug release at the end of 8 hour.

Table 2. Characterization of polymer solutions and nanofiber formulations.

Formulation Code	Characterization of Polymer Solutions			Characterization of Nanofiber Formulations			
	Viscosity (cP.s)	Conductivity (µS/cm)	Surface Tension ($mN.m^{-1}$)	Tensile Strength (MPa)	Elongation of break (%)	Work of mucoadhesion (mJ/cm^2)	Contact Angle (°)
ES	825,1±10,80	27,95±0,05	33,17±0,57	0,25±0,13	3,52±1,42	0,16±0,01	88,10±6,63
EL	2,08±0,08	36,84±0,10	27,76±0,11	0,93±0,24	13,42±6,44	0,12±0,03	99,52±5,84
EE	225±8,45	13,39±0,01	27,29±0,20	0,28±0,09	9,26±2,01	0,20±0,05	83,29±3,66

Conclusions: Eudragit-based nanofibers demonstrated suitable mechanical-mucoadhesive properties and in vitro release of 90% at the end of 8 h which prolongs the residency duration. For these reasons eudragit-based nanofibers were found to suitable for the treatment of oral ulcers.

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DEVELOPMENT AND VALIDATION OF HPLC QUANTIFICATION METHOD OF TRIAMCINOLONE ACETONIDE FOR BUCCAL DELIVERY

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Introduction: Triamcinolone acetonide, a synthetic glucocorticoid, is used in long-acting relief of symptoms of many oral inflammatory conditions, especially canker sores (1). It is known that triamcinolone acetonide is rapidly absorbed when taken orally but its oral bioavailability is 23% (2). Therefore, it is preferred to apply it by alternative means such as topical, buccal, and inhalation (3). In this study, it was aimed to develop and validate a quantification method for buccal triamcinolone acetonide.

Materials and Methods: Agilent 1100 HPLC device was used for the quantification of triamcinolone acetonide. Analyses were performed using a C18 (5 µm,4.6x150 mm) column for HPLC with isocratic elution. Detection was carried out at 238 nm with a mobile phase of Methanol:Water (70:30,v/v). The injection volume was 20 µL and the flow rate was 1.0 mL/min. The concentration range was chosen as 2.5-35 µg/mL. To validate the method, parameters such as accuracy, precision, recoverability, repeatability, etc. were evaluated according to the ICH Q2 guideline.

Results: The correlation coefficient of triamcinolone acetonide was found to be 0.9998. Triamcinolone acetonide was detected approximately at 5th minute. The high recovery and coefficients of variation of less than 1% confirm the effectiveness of the process.

Conclusions: The results showed that the developed method is a suitable method for the quantification of triamcinolone acetonide.

Acknowledgements

This study was supported by Anadolu University Scientific Research Project Foundation (Project Nu: TYL-2023-2314).

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ISOPS14 is supported within the scope of
TÜBİTAK BİDEP 2223-B Grant Program

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