Pharma-ceuticals 2024 Conference

Pharmaceuticals 2024 – The 20th Anniversary

27–29 November 2024 | Barcelona, Spain

Program and Abstract Book

Organizers

MDPI

pharmaceuticals

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Pharmaceuticals 2024 - Recent Advances in Pharmaceutical Sciences Towards a Healthy

The 20th Anniversary

Casa Convalescència
Barcelona, Spain
27–29 November 2024

Conference Chairs

Prof. Dr. Amelia Pilar Rauter
Dr. Alfredo Berzal Herranz
Prof. Dr. Mary Jane Meegan

Conference Committee

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Conference Secretariat

Dr. Ana Sanchis
Ms. Raquel Sellés
Dr. Elena González

Contents

You can find the last version of the book of abstract **here**.

Welcome from the Chairs

Welcome to Pharmaceuticals 2024, celebrating Pharmaceuticals' 20th anniversary! This meeting will showcase the art of discovering new molecules, their physical properties, and their modes of action in the search for molecular entities that can improve human health and quality of life.

Covering the newest technologies and the research areas of medicinal chemistry, natural products, organic synthesis, radiopharmaceuticals, pharmacology, toxicology, and biomolecular and glycosciences, among others, the meeting will bring together experts to present their latest findings on combatting infection, inflammation, pain, and neurodegeneration, to cite some of the relevant topics that will be discussed.

In this meeting, we encourage participation from all areas of pharmaceutical research to highlight recent advances in the field of applied chemistry in the search for novel solutions for the world's pharmaceutical needs. We will finally meet in person and will have the opportunity to bring together the younger generation, the experts, and companies to plan science and technology for the future. A roundtable will be organized to start and facilitate further discussions.

We are very pleased to announce that a ceremony is also planned to honor Prof. Jean Jacques Vanden Eynde, former Editor in Chief of Pharmaceuticals (2015-2022), in recognition of his years-long dedication to Pharmaceuticals.

Please receive our warmest invitation to join us in Barcelona from the 27th to the 29th of November this year!

Prof. Dr. Amelia Pilar Rauter
Institute of Molecular Sciences, Faculdade de Ciências, Universidade de Lisboa, Portugal

Dr. Alfredo Berzal Herranz
Department of Molecular Biology, Instituto de Parasitología y Biomedicina López-Neyra (IPBLN) CSIC, Spain

Prof. Dr. Mary Jane Meegan
School of Pharmacy and Pharmaceutical Sciences, Trinity College Dublin, Ireland

Plenary Speakers

Prof. Dr. Jesús Jiménez-Barbero
CIC bioGUNE, Bizkaia Technology Park, Spain, Ikerbasque, Basque Foundation for Science, Spain

Prof. Dr. Peter Seeberger
Max Planck Institute of Colloids and Interfaces, Director. Department of Biomolecular Systems, Free University Berlin, Professor. Institute of Chemistry and Biochemistry

Prof. Dr. Tanja M. Wrodnigg
Institute of Chemistry and Technology of Biobased Systems, Graz University of Technology, Austria

Invited Speakers

Prof. Dr. Maria Emília Sousa
Laboratório de Química Orgânica e Farmacêutica, Departamento de Ciências, Químicas, Faculdade de Farmácia, Universidade do Porto, Portugal

Dr. Nuno Manuel Xavier
Centro de Química Estrutural, Institute of Molecular Sciences, Faculdade de Ciências, Universidade de Lisboa, Portugal

Dr. Juan Carlos Morales
Senior Staff Researcher - Institute of Parasitology and Biomedicine López Neyra – CSIC, Spain

Prof. Dr. Svetlana Tsogoeva
Department of Chemistry and Pharmacy, Friedrich-Alexander University of Erlangen-Nürnberg, Germany

Prof. Dr. Irina Velikyan
Uppsala University Hospital, Uppsala, Sweden

Dr. Maria Maiarú
Lecturer in Pharmacology, School of Pharmacy; University of Reading, UK

Prof. Dr. Thierry Lomberget
Université Claude Bernard Lyon 1, UMR CNRS 5246 - ICBMS - Institut de Chimie et de Biochimie Moléculaires et Supramoléculaires, COSSBA team

Dr. Sandrine Géranton
University College London, London, U.K.

Honorary Guest

Dr. Jean Jacques Vanden Eynde
Former Head of the Department of Organic Chemistry, University of Mons-UMONS, Belgium

Abridged Program

Wednesday, 27 November 2024
12:00 – 14:00 Registration
14:00 – 18:30 // Welcome Drink: 18:30 – 20:30

Thursday, 28 November 2024
9:00 – 18:30 (Conference Dinner: 20:30)

Friday, 29 November 2024
9:00 – 16:30 pm

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You can find the detailed program here.

General Information

Pharmaceuticals 2024 - Recent Advances in Pharmaceutical Sciences Towards a Healthy Life will be held at Casa Convalescència in Barcelona 27-29 November 2024. Covering the newest technologies and the research areas of medicinal chemistry, natural products, organic synthesis, radiopharmaceuticals, pharmacology, toxicology, biomolecular and glycosciences, among others, the meeting will bring together experts to present their latest findings on combating infection, inflammation, pain, and neurodegeneration, to cite some of the relevant topics that will be discussed.

Conference Venue
Casa Convalescència
C/ de St. Antoni Maria Claret, 171, Barcelona

Registration Desk
The desk for registration, information and distribution of documents will open from 12:00h on 27 November 2024.

Certificate of Attendance
Participants of the event will be able to download an electronic Certificate of Attendance by accessing their dashboards on Sciforum.net once the event is concluded. The certificates will be found under the “My Certificates" category.

Disclaimer
Delegates will receive a name-badge at the Information Desk, upon registration. The badge must be worn prominently in order to gain access to the congress area during the event. Admission will be refused to anyone not in possession of an appropriate badge.

Insurance
The organizers do not accept liability for personal accidents, loss, or damage to private property incurred because of participation in Pharmaceuticals 2024 - Recent Advances in Pharmaceutical Sciences Towards a Healthy. Delegates are advised to arrange appropriate insurance to cover travel, cancellation costs, medical, and theft or damage of belongings.

Casa Convalescència

Casa Convalescència is located in a vibrant zone of the city, near Sagrada Familia, with easy access to urban and suburban areas of the city. It is part of the Sant Pau Art Nouveau Site. Designed by the architect Lluís Domènech i Montaner, it was built between 1905 and 1930. After housing the Hospital de la Santa Creu i Sant Pau (one of Europe's oldest healthcare centers) for more than eight decades, a restoration project commenced on the old pavilions in 2009. This process has restored the beauty of one of the iconic works of Catalonia's home-grown art nouveau, modernism.

Conference Dinner

We are excited to announce that the Conference Dinner will be held at the prestigious **Gallery Hotel**, located in the heart of Barcelona. Enjoy a delightful evening in a vibrant setting next to iconic landmarks such as **La Pedrera**, **Passeig de Gràcia**, **Casa Batlló**, and **Plaça Catalunya**.

- **Time:** Thursday, 28 November 2024 at 20.30h
- **Location:** Gallery Hotel. C/ del Rosselló, 249, 08008 Barcelona
- **Menu:** 60€. *Tickets must be purchased in advance, but you can ask for availability at the Registration Desk.*
- **Main course options:** meat, fish or vegetarian

Please let us know in your registration your main course preference and any allergies or relevant dietary restrictions.

Join us for an unforgettable dining experience in one of Barcelona's most renowned locations. We look forward to seeing you there!

More information here.

MDPI, the Multidisciplinary Digital Publishing Institute, is a publisher of fully peer-reviewed, Open Access journals with a focus on robust and rapid editorial processes. Our aim is to ensure that high-quality research is verified and made available to the research community as quickly as possible. MDPI stands at the forefront of the Open Access movement, having launched its first online journal Molecules in 1996. Today, MDPI is a leader in Open Access, publishing more than 400 journals across all research disciplines and offering publishing-related initiatives to scholars:

• Sciforum - A platform for academic communication and collaboration where scholars can set up scientific conferences.

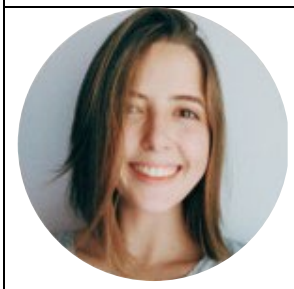
• Preprints - A multidisciplinary not-for-profit platform for rapid communication of research results before peer-review.

• JAMS - A complete manuscript submission system that incorporates all steps from initial submission to publication, including peer-review.

• IOAP – An Institutional Open Access Program that supports its members with access to MDPI's submission system, publication data and administrative processes relating to Article Processing Charge (APC) management.

If you would like more information about open access or any of our services listed above, feel free to talk to us at the MDPI booth. See you there!

Contact people during the event

	**Ana Sanchis** Email: ana.sanchis@mdpi.com
	**Raquel Sellés** Email: raquel.selles@mdpi.com
	**Cédric Spinnler** Email: cedric.spinnler@mdpi.com
	**Carmen Ruiz** Email: carmen.ruiz@mdpi.com

Emergency Information

All emergencies in Barcelona: 112

Fire brigade: 080

Accident / Ambulance: 061

National Police: 091

Local Police: 092

Abstracts — Talks

S1. Neurodegeneration

Plenary Speaker

Glycomimetics: Useful Tools and Potential Therapeutics

Tanja Maria Wrodnigg

[1] *Institute of Chemistry and Technology of Biobased Systems, Graz University of Technology, Austria*

Glycomimetics are modified carbohydrate structures which have altered physical and biological properties due to respective modifications. The modifications can be tailored towards certain biological, medicinal or technological applications. Paradigmatic examples are Tamiflu, Miglustat or AZT.

We are interested in glycomimetic structures such as iminoalditols,[i] carbacycles[ii] and *C*-glycosyl type glycoconjugates[iii] as well as C-glycosides.[iv] These glycomimetics can be applied as inhibitors for glycoprocessing enzymes, as pharmacological chaperone for the treatment of lysosomal storage diseases, as ligands for *manno*-spezific lectins such as FimH of 1-fimbriated bacteria and as probes for ligand directed chemistry profiling of activity of glycoside processing enzymes. Recently, we became also interested in synthesising polysaccharidic glycomimetics by modification of polysaccharides such as cellulose.[v] Details on the synthesis and biological evaluation of selected examples will be given.

[i]. Wolfsgruber, A.; Thonhofer, M.; Weber, P.; Nasseri, S. A.; Fischer, R.; Schalli, M.; Stütz, A. E.; Withers, S. G.; Wrodnigg, T. M. *Molecules* **2020**, *25(20)*, 4618. Thonhofer, M.; Culum, A.; Dorn, T.; Fischer, R.; Prasch, H.; Weber, P.; Stütz, A. E.; Wrodnigg, T. M. *Carbohyddr. Res.*, **2024**, *544*, 109239.

[ii]. Weber, P.; Bojarova, P.; Brouzdová, J.; Kren, V.; Kulik, N.; Stütz, A. E.; Thonhofer, M.; Wrodnigg, T. M. *Bioorg. Chem.*, **2024**, *148*, 107452.

[iii]. Hojnik, C.; Müller, A.; Gloe, T-E.; Lindhorst, T. K.; Wrodnigg, T. M. EJOC, 2016, 25, 4328 - 4337.

[iv]. Prasch, H.; Hojnik, C.; Lindhorst T. K.; Didak, B.; Landemarre, L.; Wrodnigg T. M. *Carbohydr. Res.*, **2019**, *475*, 65 – 68.

[v]. Koschella, A.; Chien, C-Y.; Tadahisa, I.; Heinze, T.; Thonhofer, M. S.; Wrodnigg T. M. *J. Macromol. Chem. Phys.*, **2019**, *221(1)*, 1900343 (1-8).

S2. Pain Care and Aging

Invited Speaker

Pharmacological modulation of the stress axis for the management of persistent pain

Sandrine Martine Geranton

[1] *Department of Cell and Developmental Biology, University College London, London, UK*

Chronic secondary musculoskeletal pain, which stems from nervous system disorders, affects 20-30% of the population. Despite its prevalence, current therapeutic strategies poorly address the complexity of chronic pain. Our previous research indicated that targeting the stress axis through pharmacological inhibition the stress driver FK506 binding protein 51 (FKBP51) could reduce sensory disturbances commonly seen in chronic pain conditions, such as allodynia and hyperalgesia. Here, we will present pre-clinical data showing that modulating the stress axis by inhibiting FKBP51 not only alleviates sensory symptoms of chronic joint pain but also improves associated affective comorbidities, including depression and sleep disturbances, that are often reported by chronic pain patients. Importantly, this treatment does not worsen the loss of joint integrity typically associated with joint disease. FKBP51 inhibition provides rapid relief from mechanical hypersensitivity, with emotional improvements emerging gradually, suggesting that affective symptoms are likely secondary to the hypersensitive state. We will also discuss the importance of early intervention for long-lasting pain relief.

Invited Speaker

Psychedelics - A New Frontier For Chronic Pain Treatment

Maria Maiarú, Tatum Askey, Gary Stephens

[1] *University of Reading*

Introduction: Chronic pain affects millions of people worldwide and presents a huge social and economic burden. Long lasting pain negatively affects the quality of life of patients and is associated with significant unmet clinical need. Management of chronic pain is difficult and clinically available drugs are often poorly tolerated and/or potentially addictive. Chronic pain patients often develop affective comorbidities, such as depression and anxiety that are frequently associated with worsening clinical outcomes
Recently there has been considerable interest in clinical potential of the psychedelic drug psilocybin, but efficacy in the treatment of chronic pain states has been poorly investigated. Evidence suggests that psilocybin can rapidly reduce measures of depression and there are some early indications that it may also alleviate chronic amputation pain and migraine in humans.
Methods: To characterise the effect of psilocybin on pain signalling we used the spared nerve injury (SNI) model of neuropathic pain. Psilocybin (0.3mg/kg and 1mg/kg)) was injected intraperitoneal (i.p.) when mechanical hypersensitivity was fully developed after surgery. We tested both the sensory 'reflex' responses to hind-paw stimulation with Von Frey hairs as well as the later 'affective' response to cold and brush stimulation. Finally, we also investigated the effect of psilocybin on gabapentin-mediated analgesia.
Results: Our results show that a single injection of psilocybin produced a long-lasting reduction in both reflex, cold and affective coping responses that develop after neuropathic injury. Beyond this, the single dose of psilocybin caused a dramatic increase in the anti-nociceptive potential of gabapentin, a widely used treatment for neuropathic pain.
Conclusion: In summary, our work demonstrates that psilocybin could be an effective tool for the management of chronic pain.

A Neurochemical, neurofunctional and psychological assessment of the emergence of chronic pain with long-COVID

Rich Harrison[1], Lydia Tidmarsh[1], Maria Maiaru[2], Eleanor Benford[1], Alex Bye[2], Gary Stephens[2], Deepak Ravindran[3]

[1] Centre for Integrative Neuroscience & Neurodynamics (CINN), School of Psychology & Clinical Language Sciences, University of Reading, UK
[2] School of Pharmacy, University of Reading, UK
[3] Berkshire Long COVID Integrated Service, Royal Berkshire Hospital, Reading, UK

Approximately 10% of COVID patients experience chronic symptoms, including pain, brain fog or debilitating fatigue. These symptoms are collectively termed long COVID. The varied symptomology of this illness implicates multiple potential mechanisms. Our own research indicates that pain is the most commonly reported symptom (Taramova et al., 2022), and the potential role of systemic inflammation has been identified as a core influence (Phetsouphanh et al, 2022).
To investigate the underlying mechanisms of pain in long COVID, this study utilised a between-groups design (n=44;21 female; Mage=50.04,s.d.=12.7y), comparing a cohort of long COVID patients with (n=24) and without (n=20) pain. Patients underwent sensory pain and psychometric assessments, alongside a resting-state magnetic resonance spectroscopy scan. The a priori hypotheses focused on the role of neuroinflammation across the anterior cingulate (ACC) and dorsolateral prefrontal (DLPFC) cortices, quantified via the glial marker myoinositol (MI; Chang et al., 2013).
The pain group were characterised by lower pain thresholds (r(44)=.37,p=.013), as well as higher depression (r(44)=-.35,p=.02), anxiety (r(44)=-.35,p=.027) and lifestyle impacts (r(44)=-.33,p=.027) scores and adverse childhood events (ACEs; r(44)=-32,p=.034).
Our findings identified lower MI concentrations in the pain group (.886ppm) vs. the no-pain group (.957ppm), when controlling for age, in the DLPFC (F(1,37)=4.32,p=.047). The MI levels within the DLPFC were also correlated with the pain threshold, with a higher threshold being associated with a higher MI concentration (r(41)=.317,p=.043). The MI concentration within the ACC was not significantly associated with the pain grouping (F(1,40)=.48,p=.49) or pain threshold (r(44)=.39,p=.067).
To investigate the function of the DLPFC, a seed-based whole-brain functional connectivity analysis identified that patients suffering from chronic pain demonstrated stronger connectivity between the DLPFC and the 1) medial prefrontal, 2) posterior cingulate cortices, 3) precuneus and 4) temporal pole.

Qualitative Audit of Pain Care Ethics Practices in a Trauma and Burn Center

Wiem Guibane, Nesrine Hagui

[1] *Center of Traumatology and Major Burns*

Introduction: This study examines how healthcare professionals at a Trauma and Burn Center understand and apply pain care ethics. It looks at their knowledge, practices, and what helps or hinders ethical care.
Methods: Researchers carried out a single-center observational study using mixed methods. For three months, they distributed a cross-sectional survey. This survey included a structured questionnaire to assess the knowledge, attitudes, and practices (CAPs) related to pain care ethics. The survey had both closed and open-ended questions. To get more in-depth insights, researchers also interviewed healthcare professionals about real-world challenges and ethical issues in managing pain.
Results: This study showed that healthcare workers had a basic grasp of pain care ethics, but how they put these into practice differed. Factors such as ongoing training and a supportive workplace helped them stick to ethical principles better [1]. However, there were significant hurdles too, such as not having enough time and too many patients, as well as not having enough resources . The in-depth data brought to light ethical problems such as trying to balance what patients need with what the institution can offer and the resources on hand.
Discussion: Our findings indicate a critical need for improved education and training to bridge the gap between the theoretical knowledge and practical application of pain care ethics [1]. Systematic changes, including policy reforms and better resource allocation, are necessary to address the identified barriers [2]. Creating a supportive organizational culture is also crucial for fostering ethical practices in pain management [3].
Conclusion: The effective integration of pain care ethics into the daily practices at Trauma and Burn Centers is vital for delivering ethical, patient-centered care. Recommendations include regular training, adequate staffing, and resource allocation to overcome barriers and enhance ethical care delivery.

S3. Infection

A Novel Enzymatic Approach for A Dandruff Treatment: Targeted Fungal Growth Inhibitors

Angelina Ivanova, Valeriya Buzova

[1] SkyLab AG, Superlab Suisse Epalinges SA, Route de la Corniche 6, 1066 Epalinges, Lausanne, Switzerland
[2] Department of Innovation Management, Faculty of Economics, M.V. Lomonosov Moscow State University, 1/46 Leninskie Gory, 119991 Moscow, Russia

Research on combating dandruff has focused on eliminating the main pathogen that triggers its development, the fungus Malassezia spp. The primary agent used to inhibit fungal growth is climbazole, which adversely affects the scalp, causing itching and irritation. The most innovative treatment is propanediol caprylate, which is structurally similar to esters, breaks down the fungus, and releases caprylic acid. However, this treatment has significant disadvantages because its antiseptic properties disrupt the entire scalp microbiome. In this study, we aimed to explore the potential usefulness of chitinase and chitosanase as anti-dandruff agents by directly targeting the fungal cell wall structures. Unlike other treatments, these enzymes degrade chitin and chitosan, the key cell wall components of Malassezia spp. These enzymes have been previously studied as biomarkers for inflammatory diseases and allergic conditions, including asthma, due to their association with the onset and progression of these disorders. They now represent a promising avenue for safe application in the inhibition of fungal growth through their enzymatic activity. In vitro experiments demonstrated that 0.25% chitinase and 0.25% chitosanase exhibited minimal fungal growth-inhibitory activity, with inhibition rates of 23.85% (p0.05) and 26.15% (p0.05), respectively. However, in combination, chitinase and chitosanase at a 0.25% concentration inhibited the growth of Malassezia spp. by 98.38% (p0.05), whereas concentrations ≥0.5% completely suppressed it. These results are comparable with those of products currently prescribed for the treatment of dandruff, suggesting these agents as a safe alternative to existing products that do not exhibit antiseptic effects by targeting fungal disruption.

A Therapeutic approach to antibiotics at the trauma center and major burns

Nesrine Hagui, Wiem Guibane, Mariem Gargouri

[1] *Center of Traumatology and Major Burns*

Introduction: Monitoring antibiotic consumption (ATB) in healthcare establishments contributes to the national policy for controlling antibiotic resistance as part of the national antibiotic stewardship program.

Materials and Method: This study describes the consumption of ATB at the intensive care unit level for burns at the trauma center and serious burns according to the AWaRe classification. This descriptive and retrospective study included all data on the antibiotic consumption of patients admitted to the burn intensive care unit over a period dating from January 1, 2019, to December 31, 2023. Systemic ATBs of class J01 of the Anatomical Therapeutic Chemical (ATC) classification were expressed in number of defined daily doses (DDJ) and related to activity according to national recommendations and the World Health Organization (system ATC-DDD,2019). Of the 180 common names of antibiotics proposed by the World Health Organization (WHO), 66 were used. The defined daily dose (DD) per 1000 presence days (DPs) was calculated per year, per patient, and overall. The data were classified according to the three WHO AWaRe groups.

Results: A total of 6632,379 DDJ/1000JP was collected over 5 years, i.e. 26.4% of the “Access” group, 55% of the “Watch” group, and 18.6% of the “Reserve” group. Over 5 years, there has been an increase in the use of antibiotics. The ratio of consumption values in DDJ/1000JP of 2021-2022 to those of 2018-2019 was overall 1.15 (2996.55/2602.61), for the “Access” group 0.48 (3424.62/6691.78), it was 0. 83 for the “Watch” group (6632.37/7963.88) compared to 0.9 for the “Reserve” group (2630.78/2907.34).

Conclusion: ATB consumption compares unfavorably to international data. This position is linked to the exceptional typology of burns (broadening the spectrum, combination of antibiotics, dosage adaptation).

S4. Immunity and Inflammation

Invited Speaker

(Radio)Theranostic radiopharmaceuticals in nuclear medicine

Irina Velikyan

[1] *Department of Medicinal Chemistry, Uppsala University*
[2] *PET-Centre, Centre for Medical Imaging, Uppsala University Hospital*
[2] *Department of Surgical Sciences, Radiology, Uppsala University*

The Radiopharmaceutical Science section is a relatively new branch of Pharmaceuticals. Its aim is to provide academic and industrial communities with open access to publications on novel radiopharmaceuticals and their applications in fundamental/applied studies in biology and medicine.
The number of nuclear medicine examinations and therapeutic procedures is rapidly increasing worldwide, reflecting the growing importance of the field in modern healthcare. This growth relies on the development and availability of radiopharmaceuticals. High demand for disease-specific radiopharmaceuticals has led to personalized treatment approaches, particularly (radio)theranostics, which use molecular imaging for diagnostics and prediction of the efficacy of therapeutic interventions on individual basis as well as for the monitoring response to the treatment.
Over the past two decades, the role of nuclear medicine in oncology has expanded significantly. The number of radiopharmaceuticals contributing to the realization of (radio)theranostics in the context of personalized medicine is increasing. Molecular imaging in nuclear medicine, presented by positron emission tomography (PET) and single photon emission computed tomography (SPECT) results in radiotheranostics when combined with endoradiotherapy. Targeting specific biomarkers turns PET and SPECT into whole-body, non-invasive “biopsies”.
A prominent example of the receptor-targeted (radio)theranostics in clinical practice is the management of neuroendocrine neoplasms (NENs) using somatostatin analogue-based radiopharmaceuticals. Following SST receptor (SSTR) targeted (radio)theranostics, prostate specific membrane antigen targeting radiopharmaceuticals spread around the world with unprecedented acceleration. Two reporting and data system classifications for PSMA- and SSTR-targeted PET imaging have been introduced to guide molecular imaging-based treatment strategies. Another notable example is the management of breast cancer targeting human epidermal growth factor receptor type 2, where quantitative PET guides the anti-HER2 targeting chemotherapy with antibody-based pharmaceuticals. This talk focuses on targeted (radio)pharmaceuticals for the imaging and treating NENs, prostate cancer, and breast cancer, demonstrating the trend towards personalized medicine in nuclear medicine

Reversal of Nickel Oxide Nanoparticle Genotoxicity in Rat Livers and Kidneys by Vitamin C

Naiha Mehmood[1], Ijaz Hussain[2], Salma Sultana[1]

[1] *GCUF, Faisalabad*
[2] *GCUG Faisalabad*

Little is known about the long-term effects of injecting nickel oxide nanoparticles (NiO NPs) into the bloodstream. This study investigated how NiO NPs affect the function of livers and kidneys in female rats, and whether Vitamin C could protect against these effects. Rats were given different doses of NiO NPs over 28 days, with or without Vitamin C. We measured markers of oxidative stress, DNA damage (using a comet assay), and liver and kidney function. The NiO NPs were confirmed to be pure crystals with an average size of 17 nanometers. As the NiO NP dose increased, the weight of the rats and their organs decreased. Higher doses were linked to increased oxidative stress and tissue damage observed under a microscope. However, Vitamin C treatment improved these outcomes, with livers and kidneys appearing more normal. The comet assay showed less DNA damage in the Vitamin C groups, indicating reduced genotoxicity. This study suggests Vitamin C protects against the harmful effects of NiO nanoparticles, providing valuable insights into the potential risks of nanoparticles and the use of antioxidants to lessen these risks.

Peptide-mediated inhibition of pericyte chaperone-mediated autophagy reveals an effective treatment against glioblastoma progression

Maria Dolores Salinas Hidalgo[1, 2, 3], Maria Luisa Molina[1, 4], Salvador Martinez[4], Jose Maria Moraleda[3, 5], Sylviane Muller[6, 7, 8], Rut Valdor[1, 2, 3]

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[2] Biochemistry, Molecular Biology B, and Immunology Department, University of Murcia (UMU), 30120 Murcia, Spain
[3] Cell Therapy and Hematopoietic Transplant Group-Internal Medicine Department, UMU, 30120, Murcia, Spain
[4] Instituto de Neurociencias-University Miguel Hernández (UMH-CSIC), 03550, San Juan de Alicante; CIBERSAM, Spain.
[5] Cell Therapy Unit, IMIB, Murcia, Spain
[6] Biotechnology and cell signalling, CNRS-University of Strasbourg, Illkirch, France/Strasbourg Drug Discovery and Development Institute (IMS), Institut de Science et d'Ingénierie Supramoléculaire, 67000 Strasbourg, France
[7] Fédération Hospitalo-Universitaire (FHU) OMICARE, Fédération de Médecine Translationnelle de Strasbourg (FMTS), Strasbourg University, 67000 Strasbourg, France
[8] University of Strasbourg Institute for Advanced Study (USIAS), 67000 Strasbourg, France

Introduction: The mechanisms of progression of glioblastoma (GB), the most aggressive brain tumor, remain poorly understood. Our team found that GB cells cause an abnormal upregulation of chaperone-mediated autophagy (CMA) in pericytes (PCs), key neurovascular unit cells, which suppresses their anti-tumor immune responses, aiding GB survival. This study investigates whether a peptide that selectively inhibits CMA in other cells can block GB-induced CMA upregulation in PCs, promoting their anti-tumor activity as a potential therapeutic strategy against GB. **Methods**: We co-cultured GB cells with peptide-pretreated PCs and assessed GB proliferation, adhesion and viability. Pretreated PC secretome in response to GB was checked by ELISA. Pretreated-PCs or the peptide alone were intravenously injected as different therapeutical strategies in a GB mouse model. **Results**: We found that *in vitro*, peptide pretreatment blocked GB-induced CMA in PCs, reducing the GB cell interaction, proliferation and survival by promoting an antitumoral and proinflammatory secretome. *In vivo* intravenous injection of peptide-pretreated PCs was efficient to promote tumor cell elimination. Direct peptide administration showed dose-dependent effects, with reduced tumor-associated inflammatory populations and not infiltration of immunosuppressive $FOXP3^+$ T cells. We found that the peptide reaching the tumor areas in the brain parenchyma was accumulated in PCs, affecting their CMA. The peptide was also found in other phagocytic cells but hardly detected in neurons. **Conclusion**: Our results identify a CMA inhibitory peptide as possible effective treatment for GB progression.

Funding: PID2020-114010RB-I00 and RYC2019-027520-I as ESF "Investing in your future", funded by MCIN/AEI/ 10.13039/501100011033; CaixaImpulse CI23- 20487.

S5. Bioorganic Molecules

In Vitro Antibacterial Activity of Mangiferin-Loaded Polymer Films Based on Hyaluronic Acid

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Global infections related to multiresistant pathogens represent real danger, both for humans and for livestock animals. Nowadays, some antibacterial drugs are forbidden by law in animal husbandry, e.g. due to the veterinary Regulation (EU) 2019/6. For this reason, natural biologically active agents with a broad spectrum of biological activities could be key molecules for effective antibacterial treatment with few side effects, but their usage is hindered by their high hydrophobicity. Biopolymer coatings (capsules) are successfully used for increasing the solubility and bioavailability of such molecules. Mangiferin, being an attractive small molecule, was selected for this study due to its wide range of therapeutic activities, including antimicrobial, antiviral, anticancer, analgesic, anti-inflammatory, etc.

Three molecular weights of hyaluronic acid (HA) were investigated in this experiment: 0.09 MDa, 1.30 MDa, and 2.48 MDa. Distilled water and dimethyl sulfoxide (50:50 v/v) were used as a solvent system. The mass ratios of HA to mangiferin were equal to 5:1, 15:1, and 25:1. The samples were obtained by applying the film-casting method to polymer solutions. The antibacterial activity of the polymer films obtained against multidrug-resistant ESKAPE bacteria (*Enterococcus faecium*, *Staphylococcus* aureus, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *and Enterobacter species*) was determined by the disk-diffusion method and the broth microdilution method.

Mangiferin-loaded polymer films showed a high level of inhibitory activity against both Gram-positive and Gram-negative bacteria. Moreover, the polymer films demonstrated antiadhesive effects, which prevent bacterial biofilm growth. The results obtained highlight the potential application of these polymer matrixes as novel antibacterial biomedical materials.

Thin polymer films with mangiferin have great significance for the further development of drug-loaded polymer systems, especially with transdermal administration. The methodology of drug loading into HA can be used for other biologically active molecules (both hydrophobic and hydrophilic).

This research was funded by the Russian Science Foundation, project number 24-23-00269. Link to information about the project: https://rscf.ru/en/project/24-23-00269/

Laser-activated magnetic-assisted delivery of bioactives using iron oxide nanoparticles - a biological perspective

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In the presented study, a system for registration of smooth muscle spontaneous contractile activity was used to investigate the biopharmaceutical behaviour of iron oxide magnetic nanoparticles and to demonstrate their potential for laser-controlled and targeted delivery of bioactive molecules. Magnetic nanoparticles consisting of an iron oxide core covered by a coating of peat extract were prepared by green synthesis. Smooth muscle strips were isolated from the corpus region of guinea pig stomach and isometrically fixed in individual organ baths filled with modified Krebs solution. The mechanical muscle activity was recorded by tensometric system. Nanosized iron oxide structures with potential therapeutic application were obtained using peat extract as reducing agent in green synthesis. The nanoparticles consist of an iron oxide core surrounded by a corona of bioactive molecules extracted from peat. Spontaneous contractile activity of the smooth muscle strips was not affected after treatment with peat-coated magnetic nanoparticles. In contrast, peat extract induced significant α-adrenergic agonist effect. After application of infra-red laser irradiation to the corona-coated nanoparticles, the release of bioactive molecules from the samples was triggered, resulting in a sharp increase in contractile activity comparable to the control assay. Infra-red laser irradiation activates the release of bioactive molecules from peat exract evidenced by modulation of the spontaneous smooth muscles contractile activity. Therefore, peat-coated magnetic nanoparticles may serve as potential carriers for targeted and controlled release of bioactive molecules.

Acknowledgements: This study is financed by the European Union-NextGenerationEU, through the National Recovery and Resilience Plan of the Republic of Bulgaria, project №BG-RRP-2.004-0007-C01.

S6. Computer Aided Drug Design

Plenary Speaker

Breaking the limits in understanding glycan recognition by NMR

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Molecular recognition by specific targets is at the heart of the life processes. The interactions between proteins (lectins, enzymes, antibodies) and carbohydrates mediate a broad range of biological activities, from fertilization and tissue maturation to pathological processes. The elucidation of the mechanisms that govern how sugars are accommodated in the binding sites of these receptors is currently a topic of interest. Thus, unravelling the structural and conformational factors and the physicochemical features that rule the interactions of these molecules is of paramount interest.

Solution NMR is unique in providing stereochemical and conformational information. Given the inherent flexibility and dynamic properties of glycans, we use NMR as key tool for deducing at atomic resolution molecular recognition processes in which glycans are involved, also assisted by a variety of synthetic, molecular biology, computational and biophysical techniques.

This presentation is focused on the application of state-of-the-art NMR methods both from the ligand and receptor's perspective to study molecular recognition processes between receptors of biomedical interest and glycans. As recent examples, key details of glycan recognition by these receptors will be shown, with special emphasis in the interactions of the human blood antigens with galectins, of sialoglycans and mimeticswith Siglecs, and of the spike glycoprotein of SARS CoV-2 with immune lectins and cell glycans.[1-6]

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Invited Speaker

From TPIs to KIs, some examples of the fight against cancer and some CNS diseases

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With an estimated 20 million cases worldwide in 2022, cancer still remains one of the most challenging public health issues to solve. In addition to surgery and radiotherapy, the development of selective and effective chemotherapeutic treatments, which would completely eradicate tumour cells with minimal side effects, is the main objective of current anticancer therapeutic approaches.

Among the different possibilities for elaborating anticancer agents, two strategies will be presented in this lecture: Tubulin Polymerization Inhibitors TPI and Kinases' Inhibitors KI.

The chemical series developed for TPIs originated from the natural product Combretastatin A-4 and has also been the source of inspiration for some of our KIs, in addition to computational and pharmacomodulation approaches.

In the second part of the presentation, concerning KIs, different targets and mechanisms of action will be presented, with particular emphasis on the interest of inhibiting DYRK1A, as this kinase is involved not only in cancerology but also in neurodegenerative pathologies such as Alzheimer's disease, another major public health problem, linked to the world's ageing population.

The Design of Drug Delivery Systems for Low Bioavailability Drugs via Compatibility Modeling: The Case of Paclitaxel

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The major issue with many anticancer active pharmaceutical ingredients (APIs) is their poor water solubility, which limits bioavailability and necessitates the use of excipients. Biodegradable polymeric excipients, with the help of nanotechnology, offer a promising strategy. In this work, the “Conductor-like Screening Model for Real Solvents” (COSMO-RS) approach was applied to predict API–polymer compatibility (i.e., the phase behavior of API−polymer systems) in silico. Subsequently, a correlation was made between the predicted API–polymer compatibility and the drug loading of nanoparticle-based polymeric drug delivery systems (DDSs). In this regard, nanoparticle-based DDSs of paclitaxel (PTX), a poorly water-soluble but highly effective anticancer API, were studied in combination with poly(lactide-co-glycolide) (PLGA) of varying molecular weights, including surface-modified PLGA with poly(ethylene glycol) (PEG). A series of nanoparticles containing 0.5, 1, 5, or 9 wt% PTX were prepared using the emulsion–solvent evaporation method. The nanoparticles underwent comprehensive characterization through advanced analytical techniques to assess their morphology, mean size, zeta potential, drug loading, encapsulation efficiency, and solid-state properties. In silico predictions showed that the molecular weight of PLGA minimally impacted PTX solubility, aligning with experiments where the maximum drug loading reached 1 wt% PTX in various PLGA molecular weights. Both the COSMO-RS-based predictions and the experimental observations agreed that PEG-modified PLGA increased PTX solubility and drug loading. The trend between COSMO-RS solubility studies and the amorphous drug loading of nanoparticles establishes the effectiveness of in silico modeling for optimizing the initial API content in polymeric nanoparticle-based DDSs.

S7. Synthetic Chemistry and Drug Discovery

Plenary Speaker

Structurally-defined Glycans as Basis for Diagnostics, Vaccines and Therapeutics

Peter Seeberger

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Most pathogens, including bacteria, fungi, viruses and protozoa, as well as cancer cells carry unique sugars on their surface. Currently, several glycoconjugate vaccines against bacteria are successfully marketed. Since many pathogens cannot be cultured and the isolation of pure oligosaccharides is difficult, synthetic oligosaccharide antigens are an attractive alternative. I will describe a medicinal chemistry approach to the development of semi- and fully synthetic glycoconjugate vaccines against severe bacterial infections, including resistant hospital microorganisms. This approach is fueled by oligosaccharides prepared by automated glycan assembly (AGA) that has been commercialized.

Vaccine programs aimed at protection from most bacteria and fungi found on the WHO list of the most critical microbial threats are underway. Vaccine candidates against *C. difficile* and *K. pneumoniae* are under development at Idorsia. Vaccine candidates against a host of other pathogens including *S. pneumoniae*, *S. suis* and *A. baumannii* are the basis for the creation of a new vaccine venture.

Synthetic oligosaccharides have given rise to monoclonal antibodies to kill cancer cells, currently developed at Tacalyx.

Invited Speaker

DNA G-quadruplex ligands with potent antiparasitic and antibiotic activity

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G-quadruplexes (G4) are DNA secondary structures, which play important roles in the regulation of gene expression in human cells. They have been proposed as therapeutic targets in cancer. At the same time, putative G-quadruplex forming sequences have also been found on the genome of parasites, bacteria and virus suggesting they could also be explored as therapeutic targets.

Here we present G-quadruplex ligands based on the naphthalene diimide (NDI) scaffold and on the drug pyrvinium (PYR). In both cases, the ligands bind strongly to G4 with notable selectivity with respect to duplex DNA. NDI derivatives prepared actually displayed antiparasitic activity in the nanomolar range against Trypanosoma brucei and Leishmania major parasites.

PYR is an anthelmintic drug recently repurposed to treat pancreatic cancer. Its mode of action entails binding to mitochondrial G4s. Our approach relates to new sugar-PYR conjugates (S-PYR), which take advantage of the “omnivorous” sugar absorption found in bacteria, in contrast to the limited number of monosaccharides absorbed by animals. In fact, several S-PYR show remarkable submicromolar activity against Gram (+) bacteria with low toxicity in eukaryotic cells and zebrafish.

Targeting Pancreatic Tumour Cell Line: Characterization of the Anti-Tumour Effects of Fluorinated ONC201 Analogues

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Introduction: Pancreatic ductal adenocarcinoma (PDAC) is one of the deadliest cancers, with a 5-year survival rate of ~11%. This statistic highlights the insufficiency of current treatments. Moreover, patients are often diagnosed at advanced stages, when metastases have usually developed. One promising candidate for targeted therapy is the imipridone ONC201, which is currently being tested in clinical trials.

Aim: The primary objective of this study was to investigate and compare the anti-tumour effects of five differently fluorinated analogues of ONC201 and to assess their cardiotoxicity.

Methods: On a PANC-1 (PDAC) cell line—(i) viability measurement: xCELLigence SP (impedimetry); (ii) cell cycle analysis: propidium iodide staining—flow cytometry; (iii) apoptosis assay: Annexin V-FITC, 7AAD staining—flow cytometry; (iv) tracking the morphometric changes: HoloMonitor M4. On HL-1 (mouse cardiomyocyte cell line)—cardiotoxicity assessment: CellTiter Glo assay.

Results: The fluorinated analogues demonstrated superior IC_{50} values compared to ONC201 (6.1 μM) at 72 hours: TBP-134 (0.35 μM), TBP-135 (1.8 μM), TBP-237 (0.14 μM), TBP-266 (0.32 μM), and TBP-353 (33 nM). At 0.5 μM after 72-hour treatment, all analogues induced G2/M phase arrest in the cell cycle except TBP-135, which required 10 μM. After 72 hours, all analogues triggered apoptosis at 0.5 μM, with most cells showing early apoptotic characteristics. Morphometric analysis also indicated apoptotic changes with a decrease in average cell area and an increase in average optical thickness. The viability of HL-1 cells remained above 50% after treatment with the molecules at 0.5 μM for 72 hours.

Conclusion: All fluorinated analogues exerted an enhanced anti-tumour effect, mediated via G2/M arrest and apoptosis, compared to ONC201, while sparing healthy cardiomyocytes. These findings highlight the potential of fluorinated ONC201 analogues as promising candidates for targeted PDAC therapy.

Funding: This research was founded by the National Research, Development, and Innovation Office (NVKP_16-1-2016-0036), by the Ministry of Innovation and Technology (EKÖP-2024-120) and by the EFOP-3.6.3-VEKOP-16-2017-00009 project.

Invited Speaker

Multi-Step Domino Reactions: *Facile Access to Bioactive Compounds for Life Sciences*

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The domino process is a powerful tool for economically and sustainably building up complex molecular architectures, which drastically reduces the number of work-up and purification steps. Recently, we developed new metal-free multi-step domino reactions and one-pot processes for waste-reducing and cost-effective preparation of versatile frameworks, which are otherwise difficult to access via traditional methods. The developed new methods engage malononitrile and other simple and readily available reagents in various domino reactions to construct new antiviral, antimalarial, and anticancer agents.

The *in vitro* tests against *multidrug-resistant P. falciparum* strains (Dd2 and K1), human cytomegalovirus (*HCMV*) and *multidrug-resistant* P glycoprotein-overexpressing CEM/ADR5000 leukemia cells revealed the selected products and corresponding artemisinin-containing hybrid compounds as highly active agents, outperforming the clinical reference drugs. Moreover, deliberately designed autofluorescent artemisinin-coumarin hybrids were not only able to overcome drug resistance, but they were also of high value in investigating their mode of action *via* time-dependent imaging resolution in living *P. falciparum*-infected red blood cells. Furthermore, a clear correlation between *in vitro* potency and *in vivo* efficacy of antimalarial autofluorescent hybrids was demonstrated. These recent results will be discussed in the talk.

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Photoswitchable carbamazepine analogs for non-invasive neuroinhibition in vivo

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A problem in systemic pharmacotherapy is off-target activity, which causes adverse effects. Outstanding examples include neuroinhibitory medications like antiseizure drugs, which are used against epilepsy and neuropathic pain but cause systemic side effects. There is a need for drugs that inhibit nerve signals locally and on-demand without affecting other regions of the body. Photopharmacology aims to address this problem with light-activated drugs and localized illumination in the target organ. Here, we have developed photoswitchable derivatives of the widely prescribed antiseizure drug carbamazepine. For that purpose, we expanded our method of ortho azologization of tricyclic drugs to meta/para and to N-bridged diazocine. Our results validate the concept of ortho cryptoazologs (uniquely exemplified by carbazopine-1) and bring to light carbadiazocine (8), which can be photoswitched between 400 and 590 nm light (using halogen lamps and violet LEDs) and shows good drug-likeness and predicted safety. Both compounds display photoswitchable activity in vitro and in translucent zebrafish larvae. Carbadiazocine (8) also offers in vivo analgesic efficacy (mechanical and thermal stimulus) in a rat model of neuropathic pain and a simple and compelling treatment demonstration with non-invasive illumination.

Studies on the Design of Tropomyosin Receptor Kinase A (TrkA) Inhibitors: A Quick Snippet from Our Lab

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Kinase inhibitors currently play a key role in various cancer and autoimmune diseases. With more than 120 approved kinase inhibitors around the world, it is considered the largest antitumor medication group. As all kinases catalyzing the same phosphate transfer reaction, there is a great similarity between their active sites. This similarity imposes a great challenge for the design of selective inhibitors within this class. Here, we will present a quick example of the work carried out in our lab in the design and evaluation of kinase inhibitors targeting Tropomyosin receptor kinase A (TrkA). Through molecular modeling techniques, two series of novel pyrimidinone and pyrazole derivatives targeting the TrkA enzyme were designed and then synthesized. The prepared compounds were screened against several cell lines and showed activities that are comparable to those of 5-fluoruracil (5-FU). Furthermore, an enzyme inhibition assay was carried out for all the prepared compounds against TrkA enzyme, and the best compound (5n) showed an inhibitory effect on TrkA with an IC50 value of 6.56 ± 0.16 μM compared to an IC50 value of 0.63 ± 0.11 μM for Sorafenib. A molecular dynamics study was also used to facilitate a better understanding of the potential interactions between these compounds and TrkA.

Synthesis of novel potentially bioactive guanidino- and guanidinopurine-containing nucleoside analogs

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Synthetic nucleos(t)ides and their analogs/mimetics have garnered significant interest in organic and medicinal chemistry due to their diverse biological properties. Several nucleoside and nucleotide analogs have found clinical applications as anticancer or antiviral drugs by interfering with nucleic acid biosynthesis[1]. Moreover, these molecules have demonstrated antimicrobial effects[2] and the ability to inhibit cholinesterases[3]. The ongoing quest for novel nucleos(t)ide analog structures that can offer innovative mechanisms of action and therapeutic opportunities remains a focal point in research.

In this communication, we present the synthesis and biological evaluation of novel 5-azido/guanidino nucleosides derived from a xylofuranose template. Additionally, we outline the synthetic route for novel guanidino-purine nucleoside derivatives, following a similar approach. Our synthetic strategy utilized diacetone-D-glucose as a precursor, involving the preparation of an acetylated 5-azidoglycosyl donor. This donor was then N-glycosylated with uracil or a purine derivative, leading to the formation of guanidine derivatives through a guanidinilization reaction. An intriguing result in the glycosyl donor precursor synthesis was the unexpected formation of an imino sugar via an intramolecular Boyer reaction.

We conducted antiproliferative assays on a panel of cancer cell lines and studied the compounds' ability to inhibit cholinesterases. Herein, we present and discuss our findings.

Acknowledgments: The authors thank the FCT for their funding through the projects UIDB/00100/2020 (https://doi.org/10.54499/UIDB/00100/2020), UIDP/00100/2020 (https://doi.org/10.54499/UIDP/00100/2020), and LA/P/0056/2020 (https://doi.org/10.54499/LA/P/0056/2020). This work was also supported by FCT through the project EXPL/MED-QUI/1017/2021 (http://doi.org/10.54499/EXPL/MED-QUI/1017/2021) and the grant CEECIND/03881/2018 (https://doi.org/10.54499/CEECIND/03881/2018/CP1553/CT0007).

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Design and synthesis of new boron-based N-acylhydrazones as potential anti-trypanosomal agents

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Chagas disease is one of the 17 neglected tropical diseases, affecting approximately 8 to 10 million people worldwide. Caused by the parasite Trypanosoma cruzi, the infection leads to various host organ lesions, including cardiomegaly, megacolon, and hepatosplenomegaly. Currently, there is no effective drug treatment for chronic Chagas disease, making its management extremely challenging. The lifecycle of T. cruzi involves several morphological transformations, mediated by specific enzymes and proteins, such as nitroreductases, squalene synthases, cysteine proteases, and cleavage- and polyadenylation-specific factors. These molecular targets are crucial for the parasite's survival and thus serve as strategic focuses for developing new treatments and molecules. In addition, the synthesis of N-acylhydrazone derivatives, an important and privileged bioisosteric group of amides combined with the boron atom, has demonstrated valuable potential in medicinal chemistry due to their chemical properties and versatility. Boron’s ability to form specific complexes, act as a bioisostere, and enhance physicochemical properties makes it a key component in the development of new drugs and therapeutic techniques today. Using computational methods, we evaluated the ligand--receptor interaction for trypanothione reductase and cruzain through molecular docking for new compounds, with Docking Scores ranging from -9.5 to -8.0 and -5.5 to -4.5, respectively, and synthesized 12 molecules which also exhibited yields exceeding 50%, reaching up to 87%. This work aims to disrupt the lifecycle of T. cruzi by inhibiting specific enzymes using the boron derivative N-acylhydrazone. The compounds are currently undergoing biological assay. Therefore, the discovery and study of new compounds are fundamental to elucidating the interactions between the molecule and its target, optimizing the understanding of specific inhibitors, and identifying key chemical groups for the treatment of Chagas disease.

Invited Speaker

Synthesis of Novel D-Glucuronamide-based Nucleosides and Nucleos(t)ide Analogs with Anticancer and Antibacterial Potential

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Nucleoside and nucleotide analogs have occupied a prominent place in medicinal chemistry owing to their ability to display a variety of bioactivities. Various molecules of these groups became relevant anticancer and antiviral drugs [1], while their antimicrobial potential has been well reported [2]. However, some drawbacks are associated with their clinical use, namely their low bioavailability and therapeutic resistance [1]. Therefore, the search for new nucleos(t)ide-like structures that may overcome such limitations remains relevant.
Our Team has been particularly focused on the use of D-glucuronamide as glycosyl template for novel nucleos(t)ide analogs, which is motivated by the significant biological properties described for D-glucuronamide-containing molecules and by the usefulness of the D-glucuronamide scaffold for enabling structural variations [3].
Encouraged by our previous findings showing the anticancer potential of N-dodecyl glucuronamide-based nucleosides [4], in this communication we disclose the synthesis of novel D-glucopyranuronamide-containing nucleoside/isonucleos(t)ide analogs comprising N-propargyl, N-dodecyl or (purinyl)alkyltriazole or alkylpurine moieties at C-6, and an anomerically-N-linked phosphoramidate group, purine/uracil unit or a 1,2,3-triazole motif, the latter of which is in some cases connected to a phosph(on)ate group. D-Glucofuranuronolactone was the precursor in the synthetic pathways that included key steps such as purine alkylation, Staudinger reaction, azide-alkyne 1,3-dipolar cycloaddition, N/O-phosphorylation, Arbuzov reaction or nucleobase N-glycosylation.
Bioactivity assays revealed some compounds showing potent antiproliferative activities in cancer cells or exhibiting significant antibacterial effects against Streptococcus pneumoniae strains, with activities comparable to those of reference drugs.

Acknowledgements:
FCT is acknowledged for funding (grant CEECIND/03881/2018 and projects UIDB/00100/2020, UIDP/00100/2020, and LA/P/0056/2020).

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S8. Natural Products as a Source of Drugs

Invited Speaker

Discovering New Antimicrobial Drugs in a Holistic One Health Approach

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One Health is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals, and ecosystems. Recognizing the importance of the environmental impact of bioactive compounds with pharmaceutical and industrial applications and the interactions between animals, pathogens and/or humans, the “safe and sustainable by design” (SSbD) approach is being integrated in the synthesis of new bioactive compounds. An unmet medical need should prioritize drug resistance that has reached critical levels, posing a public health challenge with extensive health, economic, and societal implications.

Working at the frontier of ocean knowledge and protection, at LQOF/CIIMAR, natural products (NPs) represent an opportunity to apply the SSbD concept, in a holistic approach. In this communication, design, synthesis, and biological considerations to minimize the environmental footprint of new antimicrobial small molecules will be given. To disclose their antimicrobial effects, *in silico* and HTS screening approaches were employed. An example of an integrative approach concerns the discovery of efflux pump inhibitors as antimicrobial adjuvants. The case studies presented herein are expected to contribute to a OneHeath vision in the discovery of natural products mimics with pharmaceutical applications.

Acknowledgments: This research was supported by national funds through FCT - Foundation for Science and Technology within the scope of UIDB/04423/2020 and UIDP/04423/2020 and the project PTDC/CTA-AMB/0853/2021, EXPL/CTA-AMB/0810/2021 and co-funded by FCT and COMPETE 2020, Portugal 2020 and the European Union through the ERDF.

A01. Enhanced sunscreen liniment with hematite nanoparticles for efficient photoprotection

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Introduction: The development of new effective sunscreen remains a great challenge, despite all the products on the market. Indeed, no sunscreen guarantees total protection against the sun's harmful rays; moreover, several side effects have been reported by using some products (1). Recently, iron nanoparticles have gained growing interest in sunscreen formulation and biomedical applications (2). Among the iron oxides, hematite is the most stable and presents very attractive radiative properties in the UV-visible spectrum (3).
Objective: In this work, we have set to synthesize and characterize a new sun filter containing hematite nanoparticles.
Method: Hematite nanoparticles were prepared from iron chloride by the forced hydrolysis method. An optimization of process conditions was conducted in order to select the smallest nanoparticles presenting the suitable optical properties. Nanoparticle characterization was carried out by diffraction light scattering, scanning electron microscopy (SEM), FTIR spectrometry and UV-visible spectrophotometry. Selected hematite nanoparticles were incorporated at different concentrations into a liniment. The products obtained were evaluated based on their sun protection index (SPF) and protection factor UVA (PF-UVA). The critical wavelengths were determined in vitro using a UV-visible spectrophotometer equipped with an integrating sphere.
Results: According to the preparation conditions, the hematite nanoparticles' particle size varied from 268 nm to 1,2 µm with a varying polydispersity index from 0.339 to 1. The SEM images showed an aggregate of spherical nanoparticles and the spectral analysis confirmed the existence of hematite. All the final formulations exhibited good photoprotective properties compared to the liniment placebo. The SPF indexes were higher than 15, the SPF/PF-UVA reported were below 3 and the critical wavelengths were greater than 370 nm.
Conclusion: Sunscreen liniment containing hematite nanoparticles presents interesting photoprotective properties and could be an efficient alternative to organic and chemical sun products. Pending this revolutionary progress, complementary tests are necessary to evaluate its safety and stability.

Identification and Quantification of Isoflavones in Monofloral Clover Honeys

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This study is the first to report on isoflavones with phytoestrogenic activity in different monofloral clover honeys (i.e. NSE Red Clover (*T. pratense* cultivar), NFE Red Clover (*T. pratense* cultivar), Purple Clover (*T. purpureum*), Sainfoin Clover (*Onobrychis viciifolia*)). All the clover species were grown in enclosed shade houses at the University of Western Australia's Shenton Park Field Station to enable the collection of monofloral honeys. Each enclosed shade house had a nucleus beehive placed when half of all plants were in their flowering stage. The nucleus beehives were checked regularly and frames with capped honey were transported to the laboratory and honeys were then manually removed from the frame. This approach allowed to produce monofloral honeys and therefore to derive typical phytochemical characteristics for each clover honey without potential interference from co-flowering species as might be the case for wild-harvested honeys.

Past research has demonstrated that *Trifolium* spp. exhibit a range of biological effects, including antioxidant, anticestodal, anti-inflammatory, cytotoxic, cytostatic and estrogenic activities. The latter results from the presence of isoflavones but to date, their levels in clover honeys have not been investigated despite the popularity of Red Clover as a phytomedicine for the management of post-menopausal complications.

Identification and quantification of isoflavones was carried out by High-Performance Thin-Layer Chromatography analysis. Diadzein and Genistein were identified and quantified in the four investigated clover honeys, with Red Clover showing the highest levels of both isoflavones. Moreover, some physicochemical and phytochemical characteristics (i.e. pH, colour, moisture content, total phenolic content, sugar profile) and in vitro antioxidant activity of those honeys were also determined via established protocols.

This study has identified and quantified the phytoestrogenic isoflavones daidzein and genistein in four clover honeys which should for the impetus for further research into these honeys and their potential impact on human health.

Morella spathulata (Myricaceae) as a source of antioxidants and anti-inflammatory compounds for traditional medicine in Madagascar

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Morella spathulata (Mirb.) Verdc. and Polhill, belonging to the Myricaceae family, is an endemic plant of Madagascar. It is widely used by local communities to treat a variety of disorders and pains. Despite its frequent use in traditional medicine, there is a notable lack of in-depth phytochemical and pharmacological studies on this species. Moreover, conservation efforts are critical due to threats from habitat loss and illegal logging.
This research aimed to study its antioxidant, analgesic, and anti-inflammatory properties, as well as the toxicity of methanolic extracts derived from the leaves and bark of M. spathulata (MS_L and MS_B, respectively), to better understand its therapeutic potential.
This study involved the evaluation of components such as sugars, organic acids, vitamin C, total polyphenolic content (TPC), and the main phytochemicals of MS_L and MS_B by HPLC analysis. The antioxidant capacity of the extracts was also evaluated by DPPH and FRAP (ferric-reducing antioxidant power) assays. In addition, analgesic and anti-inflammatory activities were tested by the acetic acid-induced writhing test and carrageenan-induced paw oedema in mice.
The results revealed that both leaf and bark extracts are rich in phenolics (about 81.57 mg/100 gDW) and other bioactive compounds (about 74.43 mg/100 gDW), which are related to significant antioxidant, analgesic, and anti-inflammatory activities. The interaction of key compounds, such as ferulic acid and ellagic acid, with proteins involved in pH regulation and immune response, suggests potential mechanisms for the observed therapeutic effects.
Further studies are essential to fully clarify its therapeutic potential and support its incorporation into modern medical practices.

Synthesis of New Gram-Negative Peptidoglycan Mimetics to Overcome Antimicrobial Resistance

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Bacterial antimicrobial resistance is an increasingly concerning phenomenon that is expected to lead to 10 million deaths per year by 2050. Gram-negative bacteria (GNB), which are particularly difficult to target, are amongst the most critical pathogens reported by the World Health Organization (WHO). The GNB cell envelope comprises a hydrophilic outer membrane (OM) that allows for the passage of small and polar molecules. Their peptidoglycan cell wall is composed of N-acetylmuramic acid and N-acetylglucosamine (MurNAc-GlcNAc) repeating units linked by a β-1,4-glycosidic bond prone to hydrolysis by bacterial peptidoglycan glycosidases (PGGs). The inner membrane (IM) of these bacteria is rich in phospholipids, exhibiting lipophilic properties.1,2
Deoxymonosaccharides bearing a lipophilic dodecyl unit in the anomeric position, previously synthesized and investigated by our group, already demonstrated potential in the disruption of Gram-positive bacteria membranes rich in phosphatidylethanolamine, a major IM phospholipid of some GNB.3-5
Inspired by this research, we now aim to synthesize MurNAc-GlcNAc analogues bearing a dodecyl moiety with potential against GNB. The structure of these small molecules was designed with the aum of crossing the OM, undergoing hydrolysis by PGGs in the periplasm, and releasing the dodecyl-bearing active unit to target the IM and induce membrane disruption.

Acknowledgments:
Centro de Química Estrutural is a Research Unit funded by FCT through the projects UIDB/00100/2020 (https://doi.org/10.54499/UIDB/00100/2020) and UIDP/00100/2020 (https://doi.org/10.54499/UIDP/00100/2020). Institute of Molecular Sciences is an Associate Laboratory funded by FCT through the project LA/P/0056/2020 (https://doi.org/10.54499/LA/P/0056/2020). FCT is also acknowledged for the granting of Catarina Maria's PhD Studentship 2023.01083.BD.

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Unlocking Nature's Potential: Anticoagulant and Cytotoxic Effects of Sericin and Chelidonium majus L.

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Interest in natural materials as eco-friendly alternatives to synthetics is increasing, with Sericin and *Chelidonium majus L.* (C. *majus*) emerging as promising candidates. Sericin, a biodegradable protein from silkworm cocoons, has gained attention due to its biomedical potential, despite concerns about its environmental impact when it is released into wastewater. At the same time, *C. majus*, rich in alkaloids, terpenoids, and phenolic compounds, is recognized for its therapeutic properties, including its anti-inflammatory and antioxidant effects. Both materials can potentially be used to develop anticoagulant solutions, as anticoagulant pathways are crucial for preventing thrombus formation. This study explored the synergy between Sericin and *C. majus*, focusing on their cytotoxicity and anticoagulant properties. Anti-proliferative and anticoagulant tests evaluated the effects of *Chelidonium majus* L. and Sericin (commercial and non-commercial). Their anti-proliferative potential was assessed via the Sulforhodamine B (SRB) assay on tumor and normal cell lines. Anticoagulant activity was tested using Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) assays. Various combinations and concentrations (200–3600 µg/mL) were used. The cytotoxicity results showed that most of the combinations did not inhibit tumor cell proliferation, with C. *majus* alone having a GI_{50} of about 200 µg/mL. However, the 2:2 combination of C. majus and Castelo Branco Sericin (4CS1) effectively reduced the tumor cells while maintaining normal cell growth, suggesting interactions. For anticoagulant activity, the Sericin and C. *majus* interactions varied by concentration and type. Commercial Sericin S3 was most effective in the PT assay, while Sericin S1 (from Castelo Branco) and S4 (commercial Sericin) excelled in the APTT assay. These findings suggest that these natural substances could offer sustainable, biocompatible innovations for medical applications.

Acknowledgements: FCT, Portugal, for financial support to CIMO (UIDB/00690/2020 and UIDP/00690/2020) and SusTEC (LA/P/0007/2021); national funding by FCT, P.I., through the institutional scientific employment program-contract for RC Calhelha and through the project Wastesilk (http://doi.org/10.54499/PTDC/BTA-BTA/0696/2020).

Improvement of the antioxidant effects of resveratrol via encapsulation in biopolymeric nanogels

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Oxidative stress is one of the main reasons related to the onset and progression of various disorders, such as neurological, cardiovascular, and inflammatory diseases. Natural antioxidants are widely investigated for their use in the prevention of such diseases. Resveratrol is a natural polyphenol which exhibits significant antioxidant activity via radical scavenging or by enhancing the expression of antioxidant enzymes. However, its high hydrophobicity hinders its application, leading to low bioavailability and a lack of effect. Therefore, an approach to improve these characteristics of resveratrol is needed. The aim of this research was to encapsulate resveratrol in biopolymeric nanogels prepared from citric acid and pentane-1,2,5-triol. A ratio between the drug and the polymers of 1:10 was found to be optimal for the loading. The mean diameter of the empty nanogels was 207 ± 4 nm and the ʒ-potential was negative, while the encapsulation of resveratrol led to a slight increase in the size to 220 ± 4 nm and positive ʒ-potential, which confirmed the successful entrapment. TEM analysis revealed the spherical shape of the nanoparticles. An In vitro release test showed complete release from the nanogels compared to the poor dissolution of the non-encapsulated drug. DPPH and ABTS assays revealed that the loading did not affect the antioxidant effect of resveratrol. Furthermore, in vitro cell models on neuroblastoma SH-SY5Y and fibroblast L929 cells showed that the encapsulated drug exerts improved antioxidant effects. The loading also enhanced the protective effect of resveratrol in in vitro models of oxidative stress in rat brain and liver microsomes. Therefore, the encapsulation of resveratrol in hydrophilic nanogel is an appropriate strategy to increase its solubility and enhance its antioxidant effects.

Acknowledgements: This research was funded by the European Union-NextGenerationEU, through the National Recovery and Resilience Plan of the Republic of Bulgaria, project No. BG-RRP-2.004-0004-C01.

Molecular Characterization of Therapeutic Properties of Couroupita Guianensis Bark Decoction used in Traditional Shamanic Medicine

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The Couroupita guianensis plant has been used in traditional Amazonian medicine to treat a variety of illnesses, such as skin infections, malaria, tuberculosis, pain, tumors, and inflammatory diseases. The plant is traditionally used to prepare a remedy by decoction alone or in combination with other plants. The historical use of Couroupita guianensis for treating diverse medical conditions suggests the presence of molecules with potential therapeutic properties. Investigating and analyzing these molecules at the chemical and molecular levels could lead to the development of innovative natural treatments. To scientifically validate the alleged therapeutic activities of the shamanic decoction, we prepared it under standardized laboratory conditions and compared its metabolic profiles. Due to the reproducibility of the decoction, its biological and molecular properties were analyzed in in vitro cellular systems. Promising wound healing properties were observed for the total Couroupita guianensis bark decoction and its main polyphenolic compound, which stimulated wound healing in human HaCaT keratinocytes in vitro by upregulating pro-migratory pathways while suppressing cutaneous inflammatory damage. Furthermore, the activity of the C. guianensis bark decoction was tested in a widely used in vitro model of gastric cancer, the AGS cell line, with a focus on the molecular mechanisms underlying its action. It was found that the C. guianensis bark decoction and fraction III obtained by chromatographic fractionation are highly effective in inhibiting the viability of gastric cancer cells. The activity arises from a direct inhibition of proliferation through cell cycle blockades and the activation of apoptosis.

Abstracts — Posters

Poster Session A

A01. 1,4-Diarylazetidin-2-ones: Combretastatin A-4 based anticancer agents

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The microtubule-targeting drugs paclitaxel and docetaxel are used in treating tumours in breast, ovaries, and other tissues while the vinca alkaloids vinblastine and vincristine are major drugs for the treatment of leukaemias and lymphomas. The microtubule-destabilizing stilbene Combretastatin A-4 (CA-4) binds to β-tubulin at the colchicine binding site, inhibits tubulin polymerization and demonstrates cytotoxicity towards a range of human cancer cell lines. To overcome poor bioavailability and isomerization of CA-4, we synthesised a series of conformationally restricted 1,4-diaryl-2-azetidinones using Staudinger and Reformatsky chemistry, where the ethenyl bridge of the CA-4 stilbene was replaced by a heterocyclic 2-azetidinone ring. The 3,4,5-trimethoxyphenyl Ring A of CA-4 at N-1 is retained, while the effect on tubulin binding of key substituents at C-3 (including aryl, alkyl, amino, halo, hydroxyl, phenoxy, vinyl) is investigated. 2-Azetidinones having the 3,5-dimethoxyphenyl substituent at N-1 were also studied. The antiproliferative effect of these compounds was determined in MCF-7 and MDA-MB-231 human breast cancer, HT-29 (chemoresistant colon cancer) and HL-60 (acute myeloid leukaemia). Potent Ring B modifications identified were 3-hydroxy-4-methoxyphenyl, 3-methyl-4-methoxyphenyl and 3-fluoro-4-methoxyphenyl (located at C-4 of the azetidinone), together with vinyl, chloro, phenoxy or hydroxyl substituents located at C-3. IC50 values for selected compounds were in the range 5-170 nM in MCF-7 breast cancer and 3-200 nM in chemoresistant HT-29 colon cancer cells and 2-160 nM in HL-60 leukaemia cells; they inhibited tubulin polymerisation, arrested MCF-7 cells in the G2/M phase promoted cellular apoptosis, with increase expression of pro-apoptotic proteins. X-Ray crystallographic results together with molecular modelling studies demonstrated the specific role of the C-3 and C-4 substituents in the ligand interactions with the key colchicine tubulin binding site residues.These results will facilitate design of more effective and structurally diverse azetidinones with potential for development as breast and chemoresistant colon cancer therapeutics.

A02. The Anti-inflammatory, nephroprotective, antihyperglycemic, and antibacterial activities of the hydroalcoholic extract of Porophyllum ruderale and its safety and chemical composition

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Porophyllum ruderale is an edible plant that is endemic to Mexico and used in traditional Mexican medicine. The aim of this study was to evaluate the anti-inflammatory, antihyperglycemic, nephroprotective, antibacterial, and toxic effects of the hydroalcoholic extract (MeOH:water 70:30, v/v) of the aerial parts of P. ruderale (HEPr), as well as to identify the compounds that are present in the extract. HEPr showed slight effects on LPS-NO production in macrophages and is considered a harmless species according to OECD standards; it also showed a significant reduction in glucose blood values after its oral administration in mice compared to the drug control. In addition, the values of kidney injury biomarkers in urine (urobilinogen, blood, bilirubin, ketones, glucose, protein, pH, nitrites, leukocytes, specific gravity, and microalbumin/creatinine) and serum (creatinine, urea, and urea nitrogen) of rats treated with HEPr were maintained in normal ranges in a thioacetamide-induced injury model. On the other hand, HEPr showed in vitro bactericidal effects against Escherichia coli and Pseudomonas aeruginosa and bacteriostatic effects against Salmonella typhi, Salmonella choleraesuis, Listeria monocytogenes, and Staphylococcus aureus. Finally, the organic acids 5-O-caffeoylquinic, 4-O-caffeoylquinic, and ferulic acid, as well as the flavonoids 3-O-quercetin glucoside and 3-O-kaempferol glucoside, were identified by means of HPLC as major components of HEPr.

A03. Potassium Azeloyl Diglycinate and Selected Tetracycline Antibiotics in the Topical Treatment of Acne: Novel Hydrogel Formulations

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Acne vulgaris, a common skin disease, usually has a benign course, allowing for topical treatment with fewer side effects. This study evaluated tetracycline hydrochloride and chlortetracycline hydrochloride, which are not standard topical anti-acne antibiotics , along with potassium azeloyl diglycinate (azeloglycine), an active ingredient that normalizes sebum secretion and has brightening and anti-inflammatory effects.
This study examined the effect of potassium azeloyl diglycinate on the stability of antibiotics in hydrogel formulations and their rheological properties. Additionally, the activity of the hydrogels against a model sebum layer was investigated. This activity was achieved through AMPD alcoholamine in the gels, which reacts with the acids in model sebum to form an amine soap. Three groups of products were prepared with different pH levels: slightly acidic (ca. 6.5), neutral (ca. 7.3), and slightly basic (ca. 8.2). Each group contained four preparations that varied in azeloglycine content (0% or 2%) and the presence of one of the tested antibiotics.
The stability of the antibiotics was analyzed over four weeks using HPLC. Tetracycline-containing formulations showed higher stability, except in alkaline pH gels, which showed progressive drug degradation. Hydrogels with chlortetracycline showed rapid degradation in alkaline and neutral pH, and slight instability at slightly acidic pH.
The activity against skin sebum was analyzed using a model system which reflected the follicular conditions. This activity was evident in neutral and alkaline pH formulations, with the formation of a reaction product layer at the gel–sebum boundary. Azeloglycine significantly increased this activity.
Azeloglycine, with these properties, may enhance antimicrobial treatment, increasing therapy efficacy and improving the skin condition of acne patients. Additionally, the cleansing effect of alcoholamines may allow antibiotics to reach hair follicles filled with sebum residues, where inflammation develops.

Acknowledgement: This research was funded by a Wroclaw Medical University subvention, number SUBK.D060.24.033 from the IT Simple system.

A04. Reformulating Boswellic Acids: Cyclodextrin-based Approach for Improved Solubility and Bioavailability

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Background: Cyclodextrins (CDs) are naturally occurring cyclic oligosaccharides derived from starch, known for their ability to form inclusion complexes with lipophilic compounds. These complexes may result in the increases in solubility, stability and bioavailability of the guest molecules [1]. Boswellic acids (BAs) are compounds with potential therapeutic applications in treating inflammatory diseases [2], but their use is limited due to their poor aqueous solubility (less than 0.001 mg/mL) and suboptimal pharmacokinetics. This study focused on investigating the interaction of CDs with a series of BAs isolated from the resin of Boswellia serrata to overcome these limiting properties.

Methods: The feasibility screening included various types of CDs differing in cavity size and charge. Phase solubility studies were conducted to select the best candidate for the solubilization of the four main components in the extract. Finally, effective permeation of BAs was established in vitro using the parallel artificial membrane permeation assay (PAMPA).

Results: The results generally indicated that CDs with larger cavity size and neutral charge show better interaction with BAs. Randomly-methylated-gamma-CD (RAMEG) at 5 w/v% was able to increase the solubility of BAs by well over 100-fold. However, based on the PAMPA studies, hydroxypropyl-gamma-CD (HPGCD) was able to facilitate the membrane permeation of BAs more effectively.

Conclusions: The results highlight the potential of CDs to create formulations of therapeutic agents that were previously overlooked due to poor pharmacokinetics. Our further plans include developing preformulations of BAs for various administration routes to be tested in vivo for the treatment of metritis in cattle.

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A05. Antibacterial and antifungal activities of Origanum vulgare ssp. hirtum essential oils with varying thymol and carvacrol composition

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Different Origanum species and chemotypes are widely used in agriculture, medicine, and cosmetics due to their unique chemical compositions and aromatic profiles. Oregano is widely known for its antioxidant and antibacterial properties, which perhaps explains its use in traditional medicine.
The antibacterial and antifungal activities of Oregano (O. vulgare subsp. hirtum) essential oils have been confirmed in several studies. However, the behavior of distinct oregano essential oil chemotypes, presenting varying ratios of carvacrol (CAR) and thymol (THY) which is the aim of the present study, has not yet been examined.
Antibacterial activity of the essential oils was tested in their undiluted form and in concentrations 50%, 10% and 5% in DMSO as diluent, with the paper disc diffusion method, against the pathogens Staphylococcus aureus, Escherichia coli, Salmonella enterica subsp. enterica ser. Typhimurium, Listeria monocytogenes, and Bacillus cereus. EO1 (66% THY:5% CAR) exhibited the highest activity against all five pathogens in its undiluted form, with S. aureus being the most sensitive. EO3 (4% THY: 78% CAR), EO4 (0.2% THY: 82% CAR), and EO2 (21.7% THY: 53.7% CAR) showed similar activities. Dilutions gave about similar inhibitory activities for all EOs and all pathogens with small variations.
Aspergillus niger, Byssochlamys fulva, Penicillium roqueforti, and Rhizopus stolonifer were tested for mold suppression by EOs at a 10% concentration using the paper disc diffusion method. R. stolonifer was determined to be the most sensitive mold. Among different chemotypes, those having high CAR content were more potent against P. roqueforti, while those containing THY exhibited the highest inhibition against R. stolonifer.
These results suggest that the essential oils could be employed as natural and environmentally acceptable control agents against a wide spectrum of foodborne pathogens and spoilage fungi, although their potential varies depending on their chemical composition.
This research has been co-financed by the Action “Innovation Investment Plans” of Central Macedonia, Operational Program 2021-2027 (project code MIS 5179230).

A06. Antibacterial potential of Greek oregano extract, essential oil, and distillation by-products in vitro and on working surfaces of the food industry

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Essential oils possess both antibacterial and antifungal properties. Pathogenic and spoilage bacteria can contaminate food contact surfaces and this can lead to food cross-contamination. The use of natural extracts and compounds as disinfectants has been receiving significant attention in recent years.

Greek oregano (Origanum vulgare ssp. hirtum) extract (O.E.) obtained by Ultrasound-assisted extraction, essential oil (O.E.O.), and O.E.Os by-products (hydrolate) were evaluated in vitro for their antibacterial activity against Escherichia coli, Staphylococcus aureus, Salmonella Typhimurium, and Listeria monocytogenes strains in concentrations 50%, 25%, 10%, and 5%, with the paper disc diffusion method. O.E.O. in concentration 50% exhibited the highest activity against E. coli, followed by S. aureus, L. monocytogenes, and S. Typhimurium. All dilutions showed antibacterial activity in reducing levels following the O.E.O. concentration decrease. O.E.O. was also tested in two working surfaces of food industry (stainless steel counter, teflon cutting board) after contamination. The O.E.O. in concentrations of 50%, 25%, 10%, and 5% exhibited antibacterial activity against all tested pathogens, although the lowest concentration didn't manage to kill all bacteria present. Consequently, O.E.O. 5% v/v was applied on the contaminated surfaces for 5 min and 10 min, exhibiting bacteriocidal effect. The lyophilized O.E., diluted in water, tested at the same surfaces exhibited bacteriocidal effect against all bacteria. On the contrary, the hydrolate demonstrated a disinfecting effect alone against S. aureus on the stainless surface. Without eradicating them, it also decreased the S. aureus and E. coli populations on the Teflon cutting surface.

In conclusion, O.E.O. and O.E. may be utilized as disinfectants of food-contact surfaces, while their effectiveness is depending on the target microorganisms, the duration of contact, and their concentration.

This research has been co-financed by the Action "Innovation Investment Plans" of Central Macedonia, Operational Program 2021-2027 (project code MIS 5179230).

A07. Potential Role of Hydrogen Sulfide on Copper(II) Diacetyl-di(N4-methylthiosemicarbazone) Uptake in Hypoxia

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Copper(II) diacetyl-di(N4-methylthiosemicarbazone) commonly referred to as [64Cu]Cu-ATSM, is a radiotracer that has been validated for detecting hypoxic tumors. However, its complex mechanism still remains controversial. We propose that the accumulation of [64Cu]Cu-ATSM within tumors is associated with hydrogen sulfide (H2S). To explore this hypothesis, a comprehensive in vitro cellular uptake and efflux study was performed in hypoxia and normoxia, coupled with in vivo PET imaging using rat back injection study. We also monitored changes in tumor uptake using H2S inhibitors in colon carcinoma (CT26) and murine mammary carcinoma (EMT6) tumor models. A significant increase in the cellular uptake of [64Cu]Cu-ATSM was observed in H2S-treated group compared to the control group. The in vivo PET imaging clearly showed strong signals at the H2S injection sites in rat back. Moreover, reduced uptake of [64Cu]Cu-ATSM in tumor was observed in the EMT6 and CT26 tumor models when an H2S inhibitor was injected. In conclusion, our results suggest that H2S plays some role in the retention of [64Cu]Cu-ATSM in hypoxic tumor.

Reference:

Liu, T; Karlsen, M; Karlberg, A.M; Redalen, K.R. Hypoxia Imaging and Theranostic Potential of [64Cu][Cu(ATSM)] and Ionic Cu(II) Salts: A Review of Current Evidence and Discussion of The Retention Mechanisms. EJNMMI Res. 2020, 10(1):33. https://doi: 10.1186/s13550-020-00621-5

A08. Synthesis of novel, potentially bioactive xylofuranosyl nucleoside and isonucleoside analogs

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Since their discovery over a century ago, nucleoside and nucleotide analogs have played a significant role in medicinal chemistry. These molecules exhibit a broad spectrum of physiological activities, including nucleic acid synthesis, cell division, cell signaling, and metabolism.1 They exhibit broad biological activity, being widely used in antibacterial, antitumor, antiviral, antifungal, and immunomodulatory drugs.2 The clinically approved nucleoside and nucleotide analogs are mainly prodrugs that act as nucleic acid antimetabolites.3 Recent FDA approval was obtained for the drugs remdesivir and molnupiravir, used in the treatment of COVID 19, which led to growing interest in this topic.4 Despite their great potential, there are some issues associated with their use, namely their low oral bioavailability and the resistance exhibited by cancer cells.3 Therefore, it is important to synthesize novel bioactive nucleoside/nucleotide-like molecules with the ability to overcome these problems, offering improved and alternative mechanisms of action.
In this context, we will present the synthesis of a variety of triazole 5′-isonucleosides constructed on xylofuranosyl templates. The incorporation of a triazole unit was considered to serve as a potentially neutral and stable surrogate for a phosphate group or as a nucleobase analog. The synthetic pathway involved xylofuranose precursors and utilized key steps, namely azidation, azide-alkyne 1,3-dipolar cycloaddition, N-glycosylation, and reduction, to give rise to aminomethyltriazole derivatives. In order to increase each compound's cell penetrating ability, hydrophobic moieties were installed in the molecules. In the conference, our results from this synthetic work will be presented and discussed.

Acknowledgments: The author thanks FCT for funding trough CQE and Institute of Molecular Sciences (Ref: UIDB/00100/2020 and UIDP/00100/2020., LA/P/0056/2020., EXPL/MED-QUI/1017/2021 and grant CEECIND/03881/2018, UI/BD/154822/2023).

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A09. Efficacy of Novel Herbal Compound combined with Daylight Photodynamic Therapy in Inducing Apoptosis in Human Cancer Cells

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Cancer remains a leading cause of mortality globally, presenting significant treatment challenges due to drug resistance and metastatic potential. Current treatments, including anti-cancer drugs and clinical photodynamic therapy (PDT), often face limitations, such as severe side effects and suboptimal efficacy. This study introduces a novel herbal compound comprising ethanol extracts of Taiwanese green propolis, wheatgrass, and mulberry leaves as a natural agent against cancer cells, and examines its efficacy in combination with daylight photodynamic therapy (dPDT). Taiwanese green propolis is shown to have antibacterial, anti-inflammatory, and cytotoxic properties against cancer cells, while wheatgrass and mulberry leaves exhibit promising cytotoxic effects by inducing cell cycle arrest, promoting apoptosis, and inhibiting metastasis.

The efficacy of this composition was evaluated using cell cytotoxicity assays to assess cell viability against human renal cell carcinoma (786-O) cells, both as a standalone compound and as mediators in combination with dPDT. This green and natural approach is referred to as green propolis-mediated photodynamic therapy (GPDT). High-performance liquid chromatography (HPLC) analysis identified two major components in the extract mixture. The results showed that the composition demonstrated a significant dose-dependent reduction in 786-O cell viability from 120% to 10%, with increasing doses from 0.125 µL to 8 µL, particularly when combined with dPDT at a wavelength of 570 nm. The median effective dose (ED50) values were 3.03 µL without dPDT and 1.73 µL with dPDT.

These findings highlight the potential of GPDT, a novel herbal compound with Taiwanese green propolis, to induce apoptosis and inhibit the growth of human renal carcinoma cells, particularly when paired with photodynamic therapy.

A10. Evaluation of polyphenolic content, antioxidant activity, and phytochemical profile of Origanum vulgare extracts and volatile oil

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Medicinal plants are valuable natural renewable resources. The optimal utilization of these resources is crucial for developing innovative products such as food supplements and cosmetics, which can positively impact the population's living standards.
This paper presents the polyphenolic content through both qualitative analysis (HPTLC—High-Performance ThinLayer Chromatography) and quantitative assessment (Folin–Ciocalteu assay), as well as the evaluation of antioxidant activity using DPPH and TAC assays for tincture, hot and cold hydroalcoholic extracts, and volatile oil obtained from Origanum vulgare.
The HPTLC analysis was conducted according to TLC Atlas—Plant Drug Analyses (Wagner H, Balt S. 1997). HPTLC studies were performed on 20 x 10 cm Silica Gel 60 F254 plates, with the mobile phase being ethyl acetate–acetic acid–formic acid–water (100:11:11:27, v/v/v/v) for polyphenols and vanillin–sulfuric acid for volatile oil, developed on the CAMAG HPTLC system. Caffeic acid (Rf = 0.97), chlorogenic acid derivatives (Rf = 0.79, 0.85), and flavonoid derivatives (Rf = 0.25, 0.40, 0.45, 0.61) were identified in the hydroalcoholic extracts.
In the volatile oil, the identified compounds included thymol (Rf = 0.55), caryophyllene (Rf = 0.51), linalool (Rf = 0.33), terpineol (Rf = 0.22), and terpene hydrocarbons near the surface (Rf = 0.97-0.98). The oil also contains β-phellandrene, germacrene D, ocimene, α-terpinene, and α-farnesene.
The total phenolic content was similar for the hydroalcoholic extracts obtained through hot and cold extractions and was significantly lower for the tincture.
Origanum vulgare is an important source of antioxidant compounds. Given this and the scientific results regarding its therapeutic potential, this species is an important resource for bio-products that can improve the population's health.

A11. Tracking and Evaluating Antibiotic Consumption in a Trauma and Major Burns Center

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Introduction Monitoring antibiotic (ATB) consumption in healthcare facilities contributes to the national policy of controlling antibiotic resistance within the framework of the national antibiotic stewardship program.

Materials and Methods This study describes ATB consumption in the burn ICU of the Center for Traumatology and Major Burns according to the AWaRe classification. This descriptive and retrospective study included all antibiotic consumption data for patients admitted to the burn ICU from January 1, 2018, to December 31, 2022. Systemic ATBs from the J01 class of the Anatomical Therapeutic Chemical (ATC) classification were expressed in defined daily doses (DDD) and reported per activity following national and WHO recommendations (ATC-DDD system, 2019).

Out of the 180 antibiotic names proposed by the World Health Organization (WHO), 66 were used. The defined daily dose (DDD) per 1000 patient-days (PDs) was calculated annually, per patient, and overall. The data were classified according to the three WHO AWaRe groups.

Results A total of 6632.379 DDD/1000PD was collected over 5 years: 26.4% from the "Access" group, 55% from the "Watch" group, and 18.6% from the "Reserve" group. Over 5 years, there was an increase in antibiotic use. The ratio of consumption values in DDD/1000PD for 2021-2022 compared to 2018-2019 was 1.15 (2996.55/2602.61) overall, for the "Access" group 0.48 (3424.62/6691.78), 0.83 for the "Watch" group (6632.37/7963.88), and 0.9 for the "Reserve" group (2630.78/2907.34).

Conclusion ATB consumption compares unfavorably with international data. This position is linked to the exceptional typology of burn patients (broadening of the spectrum, antibiotic combinations, dosage adaptation).

A12. Various minor factors have a significant impact during the preparation of liposomes by means of the classical thin film and hydration method

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The thin film hydration method is a common technique for liposome preparation, but its reliance on manual processes can lead to reproducibility issues. Our objective was to produce liposomes with sizes ranging from 85 nm to 120 nm, a polydispersity index (PDI) of less than 0.1, and high tumor uptake. We conducted 111 experiments to analyze the impact of the thin film morphology, the turbidity of the hydration solution, variations in the lipid composition ratios, and other factors on the liposome size, PDI, and tumor uptake. The turbidity of the hydration solution significantly influenced liposome formation. Of the 82 experiments with optimal turbidity, 88% produced liposomes larger than 85 nm, and 83% resulted in liposomes with a PDI of less than 0.1. Additionally, four instances recorded tumor uptakes exceeding 3 %ID/g. The thin film morphology is also critical. By adjusting the pressure reduction rate during evaporation, two main thin film shapes were produced: broad-band thin films and narrow bands. Broad-band-shaped thin films generally have higher tumor uptake compared to narrow-band-shaped thin films. Residual organic solvents in the rotary evaporator and inadequately cleaned flasks can significantly affect the turbidity of the hydration solution and thin film morphology. To solve this problem, a thorough cleaning protocol had to be established for both the rotary evaporator condenser and the glass flask. Cholesterol also played an important role in improving the quality and performance of the liposomes by stabilizing the lipid bilayer and forming liposomes of larger sizes. Doubling or quintupling the amount of cholesterol resulted in the liposomes exceeding 100 nm in size compared to ~95 nm under the original conditions. In conclusion, our results highlight the importance of controlling minor variables in thin film hydration methods to improve liposome quality.

A13. The Place of antibiotics from the “Reserve” group in the care of patients in the burn intensive care unit

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Introduction: Monitoring antibiotic consumption is crucial to combating resistance, improving treatments and saving money. According to the AWaRe classification of the World Health Organization (WHO), antibiotics from the “Reserve” group are used as a last resort. The objective of our work was to monitor the prescription of these antibiotics in the burn intensive care unit (RB).

Material and methods: This is a retrospective descriptive study carried out at the RB department of the Ben Arous Trauma and Severe Burn Center (CTGB) over a period of one year (from January to December 2023). All patients treated with at least one antibiotic from the “Reserve” group (tigrecycline, fosfomycin, linezolid, colistin, ceftazidime/avibactam) were included in our study. Data were collected from the Computerized Medical Record (DMI) and the STKMED software using a collection sheet.

Results: In total, 93 admitted patients were treated with a “Reserve” class antibiotic; their median age was 33 years, with a sex ratio of 2.9. Colistin was prescribed in 82.8% of cases, Tigecycline in 46.2% of cases, linezolid in 26.9% of cases, fosfomycin in11.8% of cases and the Ceftazidime/avibactam combination in only 3.2% of cases. The prescription of antibiotics was documented in 62% of cases and probabilistic in 38% of cases. The most incriminated germs were Pseudomonas aeruginosa (27.96%), Acinetobacter baumannii (19.35%) and Staphylococcus aureus (MRSA) (17.2%). The antibiotics that were most associated with the “Reserve” class in the management of the studied patients were carbapenems (59.14%), glycopeptides (23.6%) and aminoglycosides (27.96%). These results underline the crucial importance of antibiotics from the “Reserve” group in the resuscitation of burn victims, while highlighting the varied profiles of antibiotic use and combinations.

Conclusion: “Reserve” group antibiotics are widely prescribed for the management of patients in serious situations in burn intensive care. However, their use must be carefully controlled and evaluated to limit the emergence of antibiotic resistance.

A14. Evaluation of marine natural product derivatives to relieve chronic pruritus: in silico, in vitro, and pre-formulation studies

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The activation of the neurokinin-1 receptor (NK1R) by substance P has been linked to chronic pruritus, making the discovery of antagonists a promising strategy to alleviate this condition. The identification of a natural NK1R antagonist and the elucidation of NK1R's crystallographic structure facilitated the design of new NK1R antagonists. Given the connection between pruritus and inflammation, our goal was to develop novel NK1R antagonists inspired by a marine natural product, evaluate them in silico for their NK1R binding affinity (PDB6E59) and pharmacokinetic properties, assess them in vitro using skin cell lines exposed to an inflammatory stimulus, and conduct pre-formulation studies. This approach aims to create innovative compounds for the topical treatment of pruritic inflammatory skin diseases.
From a library of seventy marine-inspired ligands, eighteen compounds exhibited superior docking scores to the natural NK1R antagonist, along with favorable pharmacokinetic properties, molecular weights of up to 500, and log P values from 2.40 to 5.76. In vitro, using keratinocytes, macrophages, and fibroblasts, no relevant cytotoxicity was observed at the tested concentrations. A significant reduction in the pro-inflammatory mediator nitric oxide (NO), together with a notable decrease in inducible nitric oxide synthase (iNOS) protein levels and the absence of NO-scavenging potential, suggests the inhibition of inflammatory signaling pathways upstream of iNOS synthesis. To prepare for the incorporation of the most promising compounds into a topical formulation, pre-formulation studies were conducted, demonstrating the compounds' thermostability, photostability, and solubility.
Marine-inspired NK1R antagonists are promising for treating pruritic inflammatory skin diseases, with favorable in vitro and pre-formulation results supporting their potential for topical use.

Acknowledgments-FCT–UIDP/04378/2020, UIDB/04378/2020 UCIBIO, LA/P/0140/2020 i4HB, UIDB/04423/2020 and UIDP/04423/2020 (Group of Marine Natural Products and Medicinal Chemistry-CIIMAR), UIDB/04539/2020, UIDP/04539/2020, LA/P/0058/2020 CIBB and NORTE-01-0247-FEDER-047239, co-financed by FEDER, NORTE2020, Portugal2020. M.S.M. acknowledges FCT-10.54499/2021.05964.B.

A15. Production of quinones from Terana caerulea L.

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The fungus *Terana caerulea* (Lam.) Kuntze (Phanerochaetaceae) is a distinct one due to its unique blue color. This color is due to a mixture of molecules, mainly quinones, which has aroused great interest in the natural coloring and pharmaceutical industries. Quinones constitute a structurally diverse class of phenolic compounds with a wide range of pharmacological properties such as laxative, antineoplastic, mutagenic anti-Inflammatory, antioxidant, antibacterial, and antiviral. This work aimed to isolate and evaluate the growth conditions of *T. coerulea* to later obtain these pigments. This goal began with the evaluation of the fungu´s growth in two solid culture media (MMN and PDA). After initial growth, the fungus was exposed to ultraviolet (UV) light and different light filters to evaluate their impact on pigment production. According to the results obtained, it was possible to establish *T. caerulea* in both culture media, with pigmentation intensity and faster growth in the MMN medium. It was also found that pigmentation tests with light filters showed that the fungus grown without light filters showed more intense pigmentation, followed by fungi exposed to blue, green, red, and, finally, yellow light filters. To obtain the bioactive extract with the highest yield, purity, and stability, conventional extraction techniques (maceration) and emerging techniques (ultrasound-assisted extraction (EAU), microwave-assisted extraction (EAM)) will be used. They will be applied to define the conditions for maximizing the amount of extract and purity in the target compounds, based on response surface methodologies (RSM). These parameters will be monitored through the chromatographic profile of the quinone. Other approaches to cultivation, establishment, and stimulation of pigment formation from *T. caerulea* are ongoing, and confirmation of its bioactivities (cytotoxic, antibiotic, and antiviral).

Poster Session B

B01. Study of infectious complications linked to orthopedic interventions

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Introduction: Osteoarticular infections on materiel (OAIMs) constitute a serious secondary complication in orthopedic traumatology whose cause is multifactorial. Their occurrence seriously compromises the benefit of an orthopedic trauma intervention and is distinguished by the type of equipment used (osteosynthesis equipment, prosthesis). The objective of our work is to evaluate the incidence of OAIM, and detect incriminated germs and eventual resistance.

Materials and Methods: This was a retrospective study carried out using the nominative letters of antibiotics of patients from the orthopedic surgery department who presented with an infection on materiel and the STKMED® from January to December 2023. This study was carried out within the center of Trauma and Severe Burn Ben Arous. An information sheet was completed in order to develop a database and the results were analyzed using an EXCEL® spreadsheet.

Results: A total of 34 patients presented with OAIM. The median age was 56 years with a sex ratio of 0.8. The incidence of OAIM was 1.17%. The distribution of implants was as follows: 12 patients wearing prostheses (5 total knee prostheses, 3 hip prostheses, 2 total shoulder prostheses), while 22 had osteosyntheses. Several germs were isolated by antibiogram with a predominance of staphylococci 66.66% staph. aureus (50.61%). The prescription of antibiotics was documented in 56.94% of cases. The evaluation of antibiotic therapy showed that the most prescribed combinations were fluoroquinolones+Rifamycins at 67.64%, Glicopeptides+Rifamycins at 20.58%, and Glicopeptide+fosfomycin at 11.76%.

Antibiotic resistance was observed in 13 cases during this study. Fluoroquinolones have been linked to increasing rates of resistance, particularly against Staphylococcus aureus and coagulase-negative staphylococci (CoNS). Rifamycins are used in combination with other antibiotics to combat biofilm-forming bacteria, though resistance can still develop when used as monotherapy.

Conclusion: The management of OAIM requires an understanding of both microbial pathogens and antimicrobial therapies. Several measures should be taken to optimize the management of OAI: accessibility to modern diagnostic methods and updating guidelines for antimicrobial resistance.

B02. Consumption of colistin and fosfomycin in a burn intensive care unit

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Introduction: Antibiotic resistance represents a major challenge in the management of infections, particularly in intensive care units. Colistin and fosfomycin are often used as antibiotics of last resort. The objective of our study is to analyze the prescription profile of these antibiotics in the resuscitation of burn victims (RB).

Material and methods: This is a retrospective descriptive study carried out at an RB department of the Trauma and Major Burn Center of Ben Arous from January to December, 2023. All patients treated with fosfomycin or colistin were included.
The number of defined daily doses per 1000 days of hospitalization (DDJ/1000JH) is calculated according to WHO data from 2023.

Results: A total of 77 patients were treated with colistin (injectable 95.88 DDJ/1000JH, inhaled 137.82 DDJ/1000JH), while only 11 patients received fosfomycin (12.61 DDJ/1000JH). The prescription for colistin was documented in 63.63% of cases, while all prescriptions for fosfomycin were documented. The main organisms responsible for infections treated with colistin were Pseudomonas spp (38.9%) and Acinetobacter baumannii (32.73%). For fosfomycin, these were Pseudomonas aeruginosa (45.45%), Proteus mirabilis (27.27%), and Providencia spp (18.18%). Although these two antibiotics belong to the "Reserve" group of the WHO AWaRe classification, the delivery of fosfomycin was more restrictive due to its higher cost and requirement for a nominative letter accompanied by the antibiogram by the pharmacy service.

Conclusions: Last-resort antibiotics are widely prescribed for the management of patients in serious situations in burn intensive care. However, their use must be carefully controlled and evaluated to limit the emergence of antibiotic resistance.

B03. The Use Of Zavicefta In The Treatment Of Serious Infections In Burn Patients

Nesrine Hagui, Wiem Guibene

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Introduction: Nosocomial infections in burn patients represent a major challenge due to the increasing resistance of Gram-negative bacteria. Zavicefta (combining ceftazidime and avibactam) is used to treat these infections. This is an analysis of the clinical and statistical results of the use of Zavicefta in burn patients.

Methodology: This retrospective study analyzes the cases of six patients hospitalized in an intensive care unit for severe infections, all treated with Zavicefta in combination with other antibiotics. The results were analyzed with SPSS software to establish correlations between the different variables and clinical outcomes.

Results: A Pearson correlation test was performed that showed a significant correlation between treatment duration and clinical course (r = -0.67, p 0.05). In addition,the analysis of variance (ANOVA) revealed that the average age of patients who died (45 years) was significantly higher than that of patients who had a favorable outcome (30 years). with p 0.05. Third, patients infected with Klebsiella pneumoniae and Pseudomonas aeruginosa had a favorable outcome in 75% of cases compared to 25% for those infected with more resistant pathogens such as Pseudomonas putida and Proteus mirabilis (p 0.01). Antibiotic resistance was detected as follows: Ciprofloxacin 80% (4/5 cases), Tigecycline: 60% (3/5 cases), Meropenem: 70% (2/3 cases) and Rifampicin: 65% (2/3 cases).

Conclusion: This study highlights the importance of Zavicefta in the treatment of severe infections in burn patients. It is essential to optimize treatment duration, monitor specific pathogens and take antibiotic resistance into account to adapt therapeutic strategies in order to improve clinical outcomes in this at-risk population.

B04. Human low-molecular-weight leukocyte extract in combination with albendazole reduced infection-induced peritonitis in mice via stimulation of Th1 type of cellular and humoral immune response in mice

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Immune responses during parasitic infections are very complex processes, and the chemotherapy of tissue-dwelling parasites causes undesirable side effects. In our study, peritonitis in mice was induced with model flatworm larvae of Mesocestoides vogae and was used to investigate the effects of the drug albendazole (ABZ) and low-molecular-weight human leukocyte extract (HLE) as the adjunct therapy. Methods: Peritoneal myeloid and lymphoid cell populations were studied after termination of therapy. Results: The highest reduction in larvae was achieved by ABZ+HLE therapy, which was associated with the expansion of CD11b+F4/80midMHCIIhigh macrophages of the M1 type. Th1 polarization was confirmed by decreased gene expression for M2 markers arginase-1, FIZZ-1, Ym-1, IL-10 and transcription factors STAT-3 and STAT-6. The expression of the M1 marker iNOS was up-regulated as well as the INF-γ receptor, STAT-1 and IL-12. The lymphoid cell population diminished to approximately 30% of inflammatory cells due to the expansion of myeloid-derived cells with suppressive properties. Combined therapy resulted in the highest upregulation of Tbet m-RNA expression and downregulation of Foxp3, and GATA in lymphoid cells. Peritoneal CD19+B1 lymphocytes were gradually replaced with CD19+CD138+ plasmablasts and CD19-CD138+plasma cells in all infected and treated groups producing IgM and IgG subclasses of antibodies to excretory/secretory (E/S) and somatic parasitic antigens. Drug-modulated antibody secretion profiles and HLE alone, and in combination with ABZ, stimulated the production of Th1- associated IgG1 and IgG2a antibodies while supressing IgM antibodies to E/S antigens. A Western blot analysis of peritoneal exudates from infected and treated mice revealed differential expressions of individual antigens. Conclusions: ABZ and HLE therapy activated the proinflammatory Th1 type of cellular and humoral immune response, resulting in balanced Th1/Th2 immunity and the highest efficacy in infected peritoneal cavities in mice. Acknowledgement: This study was funded by the Scientific Grant Agency, grant number APVV – 17-0410 and VEGA no. 2/0033/21.

B05. A Photopharmacological Approach: Designing Azobenzene-Modified Photoswitchable Agents for the Treatment of Amyotrophic Lateral Sclerosis

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Pharmacotherapy frequently faces significant challenges due to inadequate drug selectivity, which can lead to adverse effects, environmental harm, and resistance development. Photopharmacology addresses these issues by integrating photoswitchable groups into the molecular frameworks of bioactive compounds. These photosensitive elements enable the application of light as an external control to precisely regulate the pharmacological effects, offering exceptional control over both timing and localization. Photopharmacology might therefore be combined with chronotherapy, which is the study of biological rhythms and their impacts on health, and presents a potential avenue for treating amyotrophic lateral sclerosis. This study investigates the therapeutic potential of clock gene-related interventions, specifically targeting genes that regulate biological rhythms, in the management of neurodegenerative diseases. Among the key clock genes, nuclear receptor subfamily 1 group D member 1 (NR1D1) has been identified as crucial in the pathogenesis of such disorders. In this research, photoswitchable derivatives of FDA-approved drugs used for amyotrophic lateral sclerosis were computationally modified with azobenzene motifs. The impact of these modified drugs on NR1D1 regulation was assessed through molecular docking and simulation techniques via AutoDock Vina and GROMACS 2023.2 software. Molecular structures were specified using canonical SMILES strings, and ligand preparation was conducted using ChemDraw Pro 12.0 and LigandScout 4.4.5 software. The findings indicated that the planar (E) configurations of the azobenzene switches demonstrated significantly higher (P0.001) binding affinities to NR1D1 and more stable docking complex energies compared to the globular (Z) configurations and drugs without azobenzene modifications. Consequently, incorporating photoswitchable elements into FDA-approved drugs might enhance outcomes in chronobiological therapies. This study offers foundational data that support further exploration through in vitro and in vivo studies. The results highlight the necessity of additional research to determine the clinical and experimental efficacy of this innovative approach.

B06. Development Of Solid Lipid Nanoparticles For Enhancement Of Transdermal Delivery Of Anti-Inflammatory Drug Properties: In Vitro And In Vivo Evaluation

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The objective of this study is to develop an enhanced transdermal formulation of ketoprofen loaded in solid lipid nanoparticles to improve its effectiveness in treating inflammatory conditions when applied topically. This study investigated the impact of additives such as stearic acid, Tween 80, and varying amounts of water or alcohol on formulation stability using a mixture design. Particle size distribution based on number and intensity was evaluated, and the optimized formulations were further characterized and assessed for pharmacodynamic activity in comparison to commercially available FASTUM gel 2.5%. The optimized solid lipid nanoparticles exhibited a particle size of 7 ± 0.66 nm (PDI=0.341) and a zeta potential of -14.2 ± 0.61 mV, indicating good stability. Significant reductions (P 0.05) in paw thickness were observed compared to both the commercially available gel (36.28% reduction) and the pure drug group (44.04% reduction). Moreover, the optimized formulations demonstrated substantial decreases in PGE 2 and TNF-α levels by 55.6% and 58.4%, respectively, compared to the carrageenan-induced inflammation group. The developed transdermal ketoprofen formulation exhibited promising results in reducing inflammation, thereby enhancing its potential as an effective treatment for inflammatory skin diseases.

B07. New Pyrazoles and Diazepines as Curcumin bioisosters with antioxidant and neuroprotectant activity

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Neurodegenerative diseases are of mayor concern today due to their high incidence among an increasing and aging population. Alzheimer's and Parkinson's diseases are more prevalent, but others like frontotemporal dementia, Lewy body dementia, amyotrophic lateral sclerosis, and multiple sclerosis show a constant increase [1].
Despite the research efforts made by the scientific community to find new effective therapies to cure those diseases, there is not a successful drug or treatment for any of them. Only some old drugs are being used to alleviate symptoms [2].
Using curcumin as an in vitro well-validated antioxidant and neuroprotectant chemotype, and as a continuation of our research on the evaluation of new asymmetrical 1,3-diketones [3], our efforts have been focused on the exploration of this chemotype through two new chemical families, pyrazoles [4] and diazepines [5], with biological activities that overcome the stability, solubility, and bioavailability issues of curcumin.

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Acknowledgements: Thanks are given to the UNED and Universidad CEU San Pablo for their support.

B08. Impairment of autophagy as a pathogenic mechanism in chemotherapy-induced neuropathy

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Introduction: Autophagy is a physiological mechanism in the cell's life contributing to protein and organelles degradation, cellular remodelling and survival. An imbalance in this process can impact basal functions leading to cellular dysfunction.
Chemotherapy-induced peripheral neuropathy (CIPN) is a debilitating and painful condition that develops as an adverse effect of antineoplastic drugs. Chemotherapy treatments are thought to induce molecular changes in neurons in the nociceptive pathways that might lead to CIPN and some of these molecular changes have been linked to autophagy alteration.
Aim of this study was to investigate the consequences of paclitaxel treatment on the autophagic process.

Methods: Male and female C57BL/6 and GFP-LC3 mice were treated with Paclitaxel (PTX) (4mg/Kg) on alternating successive days (day 0, 2, 4 and 6). We tested the sensory 'reflex' responses to hind-paw stimulation with Von Frey hairs or dynamic aesthesiometer plantar test. Finally, we also investigated the response to thermal stimulation. Protein levels of the main autophagic markers LC3, Beclin 1 and p62 were investigated by western blot analysis together with immunofluorescence and image analysis in the dorsal horn of mice.

Results: PTX treatment induced prolonged hypersensitivity in male and female mice. The hypersensitivity was associated with upregulation of LC3 levels in the L4-L5 portion of the spinal cord 7 and 21 days after the first injection of Paclitaxel. However, no increase in LC3 levels were observed 14 days after the first injection, but an accumulation of p62 was recorded, suggesting that autophagy may be impaired at this time point. Finally, injection of Beclin 1- activating peptide reversed paclitaxel-induced mechanical hypersensitivity in adult and aged mice.

Conclusions: Our data suggest that a dysfunction of the autophagic mechanisms may leads to CIPN and prompts for further investigations on the role of this degradative pathway in pain processing.

B09. Clinical significance of microbiota changes under the influence of psychotropic drugs

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The proper functioning of the microbiota is key to the positive effects of some drugs used in medicine. Pharmacotherapeutic agents can modify the microbiota, which consequently affects its functioning. Here, I have compiled comprehensive data showing that nearly 25% of drugs administered to humans have antimicrobial effects, such as antidepressants and antibiotics. Cusotto and Maier et al. observed during their study that the effect of psychiatric drugs on changes in the composition of the gut microbiota leads to control over symptoms of mental illness. Thus, the gut microbiota influences stress resistance and the risk of developing psychiatric disorders, plays an important role in the therapeutic process by having no effect on drug metabolism, and likely modulates the severity of psychiatric symptoms. On the other hand, antibiotics (e.g., isoniazid, minocycline) cause changes in the psychiatric phenotype, and their side effects include neurological and psychological symptoms, supporting the hypothesis that the gut microbiota can affect the functioning of the CNS. By far, greater potential lies in the use of psychobiotics. Psychopharmacotherapy, which, among other things, blocks dopamine D2 receptors, also has a bactericidal effect. The alleviation of clinical symptoms of mental illness may depend not only on the known pharmacological effects of psychotropic drugs but also on the interaction of these drugs with the gut microbiota. During treatment, metabolic disorders resulting from the administration of drugs are observed, which may be related to disorders of the microbiota. Severe metabolic disorders are a reason for discontinuing psychopharmacological treatment or changing the drug being administered, despite its good effect on symptoms of psychiatric disorders. Supplementation with appropriate probiotic strains may alleviate the discomfort associated with metabolic disorders and support the positive effect of the drug. The data collected highlight the need for further research to analyse the function of the gut microbiota.

B10. Changes in the profile of fatty acid derivatives under the influence of long-term caloric restriction

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Caloric restriction (CR) is a dietary intervention based on the limitation of calories relative to the basic energy needs of an organism. The use of CR changes the metabolism intensity, causes changes in the functioning of the endocrine and sympathetic systems, and influences the expression of genes in muscle, heart, and brain cells. During the use of CR, there is a transition from the supply of carbohydrates to an increased metabolism of fats. Fatty acids—depending on their molecular structure—may be more or less susceptible to the influence of free radicals. Oxidation (peroxidation) contributes to the production of metabolites (including HETE and HODE), of which some are involved in inflammation.
The aim of this research was to analyze the influence of long-term CR on the contents of fatty acid derivatives with a pro- or anti-inflammatory character.
The research was conducted on mice of the C57BL/6 race. During the 8-month-long experiment, the study group of mice received food with 30% caloric restriction. Fatty acid derivatives were isolated using SPE (C-18)-type columns and then analyzed using liquid chromatography.
Of the studied fatty acid derivatives, a decrease in concentration was mainly observed for those with anti-inflammatory properties (resolvin, LTX A4 5S, 6R, marezines, 13S HODE, 9S HODE, 17RS HDHA). However, there was no increase in the concentration of pro-inflammatory eicosanoids. It should be determined which of the changes occurring at an epigenetic level contribute to the synthesis of enzymes that are responsible for the production of pro-inflammatory factors.

B11. Exploring Formoterol Aerosol Characteristics: Comparative Study of Commercial DPI Devices in Respiratory Disease Management

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Chronic respiratory diseases such as asthma and chronic obstructive pulmonary disease (COPD) are global health challenges, often characterized by persistent inflammation and airflow obstruction. Effective treatment of these conditions involves a combination of anti-inflammatory and bronchodilatory medications. Formoterol, a long-acting β2-agonist (LABA), is a key therapeutic agent that helps manage bronchoconstriction by providing prolonged bronchodilation. However, the effectiveness of formoterol is highly dependent on the efficient delivery of the drug to the lower respiratory tract, which is influenced by factors such as the aerodynamic particle size distribution (APSD) and the type of dry powder inhaler (DPI) used.
This study aims to investigate the APSD of commercially available formoterol-containing formulations utilized in the management of asthma and COPD. The research focuses on evaluating several DPI devices, including Zonda ®, Handihaler ®, Cyclohaler ®, and Breezehaler ®. By comparing these devices, the study assesses how inhaler design impacts the aerodynamic properties of the aerosol and, consequently, the deposition of formoterol in the respiratory tract.
To measure APSD, a Next-Generation Impactor (NGI) was employed, allowing for the precise classification of aerosol particle sizes. This method offers insights into the size range of particles that can effectively reach the lower airways and exert therapeutic effects. In addition, Ultra-Performance Liquid Chromatography (UPLC) was used to quantify formoterol in various particle size fractions, providing a comprehensive analysis of the drug's distribution in different regions of the respiratory tract.
Given that particles in the 1-5 μm range are optimal for lung deposition, this study explores the significance of particle size distribution for enhancing drug delivery and improving clinical outcomes in asthma and COPD management. The findings will contribute to ongoing efforts to optimize inhaler technology and enhance patient outcomes by ensuring more efficient and targeted delivery of formoterol to the lungs.

Funding: The research was financed by an R&D grant financed by the LIDER project by the National Center for Research and Development (Poland), Project number: 0276/L-12/2020

B12. Evaluation of Aerodynamic Particle Size Distribution (APSD) of Fluticasone in Commercial Dry Powder Inhalers (DPIs) for Optimizing Asthma and COPD Therapy

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Respiratory diseases such as asthma and chronic obstructive pulmonary disease (COPD) are chronic inflammatory conditions that require effective therapy to control inflammation in the airways. Fluticasone, a glucocorticosteroid, plays a key role in suppressing the inflammatory response and modulating the immune system in patients with these conditions. Proper delivery of the active substance to the lower respiratory tract is essential for the effectiveness of treatment, which depends on the aerodynamic particle size distribution (APSD) generated by dry powder inhalers (DPIs).
The aim of this study was to evaluate the APSD of commercially available fluticasone-containing medications used in the treatment of asthma and COPD, employing various capsule DPIs, including Zonda(R), Handihaler(R), Cyclohaler(R), and Breezhaler(R). This study aimed to determine how different devices influence the effectiveness of fluticasone delivery to the lungs, which is crucial in bronchial inflammation control and improved respiratory function.
This study was conducted using a Next-Generation Impactor (NGI) for precise analysis of the aerodynamic particle size distribution and an ultra-high-performance liquid chromatograph to quantify the fluticasone in different aerosol fractions. Particular attention was given to the particle fraction with an aerodynamic diameter of 1-5 µm, which is critical for effective delivery to the lower respiratory tract.
The results revealed differences in APSD among the analyzed inhalers, impacting the effectiveness of fluticasone delivery to the lungs. Inhalers such as the CYCLOHALER and BREEZHALER demonstrated higher efficiency in producing particles in the optimal size range, while other models, like the HANDIHALER, generated larger particle fractions, potentially reducing therapeutic effectiveness.
This study provides valuable insights into the technical parameters of DPIs and their influence on the efficiency of fluticasone inhalation therapy, which can assist in optimizing treatment for patients with asthma and COPD and controlling inflammation in the airways.

Funding: The research was financed by an R&D grant financed by the LIDER project by the National Center for Research and Development (Poland), Project number: 0276/L-12/2020

B13. Trends in Antibiotic Consumption in the Orthopedic-Trauma Department of a Trauma Center

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Introduction: Antimicrobial resistance remains a critical global health issue, particularly in hospital settings, where patients are vulnerable to infections. The WHO's "AwaRe" classification categorizes antibiotics into three groups, "Access," "Watch," and "Reserve", to promote rational use. This study aims to track antibiotic consumption in the orthopedic-trauma department and underscore the implications of their misuse.

Methods: This descriptive retrospective study was conducted at the Trauma and Major Burns Center of Ben Arous over four years, from January 2020 to December 2023. Antibiotic consumption was expressed in Defined Daily Doses per 1000 hospital days (DDJ/1000JH) and calculated using Excel. Data were collected from the STKMED software, including patient demographics and exclusion criteria for a comprehensive understanding of the study population.

Results: During the study period, antibiotic consumption from the "Access," "Watch," and "Reserve" categories accounted for 40.8%, 53.5%, and 5.7% of the total consumption, respectively. Among the "Access" group, amoxicillin/clavulanic acid was the most prescribed, increasing from 54.33 DDJ/1000JH in 2020 to 254.24 DDJ/1000JH in 2023, reflecting a 368% growth. In the "Watch" group, injectable ciprofloxacin was most utilized (28.3%), rising from 45 DDJ/1000JH in 2020 to 106.3 DDJ/1000JH in 2023. Conversely, rifampicin consumption decreased from 91.8 DDJ/1000JH in 2020 to 42.1 DDJ/1000JH in 2024. In the "Reserve" category, significant increases were noted for fosfomycin (4 g) and linezolid (600 mg) in 2023.

Discussion: The increase in "Watch" and "Reserve" antibiotics highlights the need for careful prescribing. Educational interventions for practitioners on the WHO guidelines are critical for mitigating resistance and improving patient outcomes.

Conclusion: This study emphasizes the importance of prudent antibiotic use and adherence to the WHO guidelines to preserve efficacy and combat antimicrobial resistance effectively.

B14. Management of Multi-Resistant Bacterial Infections in Burn Intensive Care Units: An Epidemiological Study

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Introduction: Infections caused by multi-resistant bacteria (MRB) pose significant challenges in burn intensive care units due to the heightened vulnerability of patients. This study aims to analyze the epidemiological profile of these infections, identify the pathogens involved, and evaluate the antibiotic therapies administered.

Methods: A prospective study was conducted in the Burn Unit of the Trauma Center and Major Burns of Ben Arous (CTGB) from January 1 to March 15, 2024. All patients with MRB infections, confirmed by antibiogram, were included.

Results: Twenty-five patients were identified with MRB infections. The median age was 36 years, with a sex ratio of 2.1. The average duration of hospitalization before infection onset was 15.93 days. The pathogens isolated included Acinetobacter baumannii (27.66%), Klebsiella pneumoniae (14.89%), and Proteus mirabilis (12.76%). The most common sites of infection were pulmonary (34.04%), septicemia (27.66%), and catheter-related infections (19.89%). Antibiotic therapy included colistin (29.51%), tigecycline (26.23%), and fosfomycin (18.03%), while carbapenems were utilized in only 13.1% of cases due to carbapenemase production. Clinical outcomes were favorable in 64% of cases, with a mortality rate of 36%.

Discussion: The emergence of MRB in burn patients presents significant clinical challenges. These patients are particularly susceptible to infections due to compromised skin and prolonged hospital stays, leading to higher infection rates (1). The prevalence of Acinetobacter baumannii is notable, often linked to increased mortality (2). The limited use of carbapenems reflects the rising prevalence of resistant organisms (3). The effective management of MRB infections requires continuous monitoring, prudent antibiotic use, and robust infection control measures (4).

Conclusion: Our study underscores the urgent need for ongoing surveillance and effective antibiotic stewardship in burn units to combat MRB infections, improving patient outcomes and reducing mortality rates. Continued research is essential to develop new strategies for managing these challenging infections.

B15. Assessment of the Implementation of a New Tool for Medication Supply Management

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I**ntroduction:** Effective management of pharmaceutical supplies is essential for ensuring patient safety, maintaining product quality, and minimizing financial strain. In 2019, efforts were initiated to optimize our supply chain by reducing order frequency while upholding safety and financial standards. The aim was to evaluate the long-term impact of these strategies implemented three years ago.

Materials and Methods: Our institution employs a calendar-based approach for drug procurement, with fixed-order days and variable quantities. Medications in stock are categorized based on their consumption value, using the ABC method to establish ordering intervals: Class A (80% of annual value, ordered every 7 days), Class B (next 10%, every 14 days), Class C (following 5%, every 28 days), and Class D (remaining 5%, every 56 days). The categorization was initially updated in summer 2021 and again in January 2023. We conducted an analysis of various metrics, including order volumes, line items, and urgent order frequencies.

Results: During the latest assessment, adjustments were made to the ordering intervals for 12% of the medication categories. However, the overall distribution across classes remained consistent compared to 2019: Class A (5.2%), Class B (7%), Class C (9.3%), and Class D (78.5%). Between 2019 and 2022, there was a notable reduction of 24% in order line items, a 46% decrease in urgent orders, and a 10% decline in total orders.

Conclusion: These strategies have significantly improved our supply management by reducing order frequency, leading to a corresponding 16% decrease in the variety of medications ordered and thereby lessening the financial impact of inventory management. Continuous updates to electronic records, periodic reviews of order intervals, and adherence to safety standards tailored to critical product categories are crucial for sustaining these improvements, guided by decisions from the Medication and Sterile Medical Devices Commission.

B16. The Role of the Pharmacist in Therapeutic Education for Elderly Diabetic Patients

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Introduction: Therapeutic patient education (TPE) is a pedagogical approach that ensures the transfer of knowledge between the patient and the caregiver. Its purpose is to help patients acquire and maintain the daily skills necessary to adequately manage their condition.

Materials and Methods: A statistical survey was conducted using Google Forms over one month, targeting 40 hospital and community pharmacists. The survey aimed to highlight the impact of pharmacists in the therapeutic education of elderly diabetic patients. Data collection was performed using the same platform.

Results: Out of 40 pharmacists, 21 responded to the survey, with 83.8% being hospital pharmacists and 16.7% being community pharmacists. Among the 21 pharmacists surveyed, 44.4% were aware of therapeutic education programs, highlighting the significant role of pharmacists in these programs, with 70% recognizing their key role. The role of the pharmacist in patient education was confirmed by 85.7% of respondents, despite challenges such as a lack of time (66.7%), patient resistance (28.6%), and a lack of pharmaceutical training (28.6%).
A significant 90.5% of pharmacists indicated that the layout of their workplace hindered the conduct of therapeutic sessions. Additionally, 57.1% lacked information on the short- and long-term complications of diabetes. A substantial 95.2% of pharmacists believed that certain elderly diabetic patients would benefit from a therapeutic education program, particularly those struggling with adherence (76.2%), those needing lifestyle changes (71.4%), and those whose caregivers should be involved in their care (52.4%). Finally, 90.5% of pharmacists expressed an interest in receiving training in therapeutic education.

Conclusion: This survey highlighted the crucial need for a pharmaceutical educational approach for diabetic patients. Pharmacists can play a pivotal role in TPE programs, collaborating with other healthcare professionals. However, their involvement requires adequate training and regular evaluation of their activities to optimize multidisciplinary care for elderly diabetic patients.

B17. Nano-in-micro drug delivery system for nasal administration of deferiprone in neurodegenerative disorders

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Due to the steadily ageing population, the rapidly increasing number of people affected and their severely debilitating nature, neurodegenerative diseases are considered an extremely serious global health problem. It is well-known that metals such as iron and copper catalyze oxidation-reduction processes in the body. Longer lifespans lead to the accumulation of iron in various parts of the brain, although this is not always associated with toxicity. Iron plays a crucial role in the physiological functions of the brain, being involved in mitochondrial respiration, myelin and neurotransmitter synthesis. Deferiprone, which is an iron chelator with short biological half-life, has been indicated as a treatment modality in neurodegenerative disorders such as Alzheimer's and Parkinson's disease. However, it leads to agranulocytosis and neutropenia with prolonged therapeutic course. Its inclusion in sustained release dosage forms may reduce the frequency of administration. On the other hand, when administered by an alternative route of administration, such as the nasal route, systemic exposure to deferiprone will be reduced, reducing the occurrence of adverse effects. Direct nose-to-brain delivery has been raised as a non-invasive strategy to deliver drugs to the brain, bypassing the blood-brain barrier. The aim of the study was to develop and characterize nanocomposite microspheres suitable for intranasal administration by combining nano- and microparticle-based approaches. Nanoparticles with an average particle size of 213 ± 56 nm based on the biodegradable polymer poly-ε-caprolactone were developed by solvent evaporation method. To ensure the deposition of the particles in the nasal cavity and avoid exhalation or deposition into the small airways, the nanoparticles were incorporated into composite structures of sodium alginate obtained by spray drying. Deferiprone demonstrated sustained release from the nanocomposite microspheres and high iron-chelating activity.

Acknowledgements: This study is financed by the European Union-NextGenerationEU, through the National Recovery and Resilience Plan of the Republic of Bulgaria, project №BG-RRP-2.004-0007-C01.


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