



The 1st International Electronic Conference on Medicinal Chemistry and Pharmaceutics

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The 1st International Electronic Conference on Medicinal Chemistry and Pharmaceuticals

1–30 November 2025 | Online



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Welcome from the Chair

Dear Colleagues,

We cordially invite you to join us at the **1st International Electronic Conference on Medicinal Chemistry and Pharmaceutics (ECMC-P 2025)**, sponsored by MDPI's open access journals *Pharmaceutics* and *Pharmaceuticals*.

This platform seeks to provide a forum for discussion for scientists from around the world to share recent developments and innovative ideas in medicinal chemistry and pharmaceutics. This will allow students, researchers, and experts to share their latest theories, results, models, and applications within this multidisciplinary area of knowledge. This is an entirely online conference that will be held in November at <https://sciforum.net/event/ECMC-P2025>. No registration fee will be charged to participants, and an added advantage is the lack of cost for flights, hotels, etc.

The conference will be organized around the aims and scope of the journals *Pharmaceutics* and *Pharmaceuticals*, which includes the following general topics:

- Small molecules as drug candidates
- Biomolecules, natural products, phages, and cells as therapeutic tools
- Biological targets and biomarkers
- Radiopharmaceutical sciences, radiochemistry, (hybrid) imaging, and nuclear medicine
- Nanotechnology
- Pharmacokinetics and pharmacodynamics
- Pharmaceutical preparations and drug delivery

Researchers are invited to provide a short abstract (250 words maximum without figures and references) online, through this [link](#) from now until **21 September 2025**.

Each participant can submit only one abstract as a presenting author and a maximum of three submissions per research group (each author can only sign a maximum of three contributions). An institutional email address is required to submit contributions. The authors will be notified in October 2025 about the acceptance status of their abstract(s). At that point, they will be asked to present their work (in English) as a poster, a slideshow, or a video using the templates provided by the conference (see Instructions for Authors). All accepted submissions will be displayed online and be open for discussion, comments, and questions during the entire conference at conference website on **1–30 November 2025**.

All participants will be invited to submit a full paper describing their work. The papers will be peer-reviewed and, upon acceptance, published in a Special Issue. A 20% discount on the article processing charge will be applied.

The scientific committee will select the most outstanding works, which will be rewarded with grants offered by the sponsoring journals, *Pharmaceutics* and *Pharmaceuticals*.

We look forward to engaging in exciting discussions and hearing new ideas and perspectives from experts in the field. All participants are welcome to join the online conference.

Kind regards,



**Prof. Dr. Maria
Emília Sousa
Conference Chair**

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Pharmaceuticals (ISSN 1424-8247) is an international scientific journal of medicinal chemistry and related drug sciences.

Our aim is to publish updated reviews as well as research articles with comprehensive theoretical and experimental details. Short communications are also accepted; therefore, there is no restriction on the maximum length of the papers.

The multidisciplinary journal welcomes manuscripts covering a wide range of aspects involved in drug discovery and development. The following topics are considered:

Small molecules as drug candidates: drug discovery, drug design, medicinal chemistry, combinatorial chemistry, SAR, structure-property correlations, molecular modeling, pharmacophore, and bioinformatics;

Biomolecules, natural products, phages, and cells as therapeutic tools: peptides, aptamers, glycans, antibodies, extracts, bacteriophages, and stem cells;

Biological targets and biomarkers: enzymes, receptors, membranes, genes, ion channels, inhibitors, agonists, antagonists, neurons, binding affinity, biofilms, bacteria, viruses, parasites, and protein–protein interactions;

Radiopharmaceutical sciences, radiochemistry, (hybrid-)imaging, and nuclear medicine: radiopharmaceuticals, radiotracers, fluorescent dye labeled tracers, contrast agents, PET/CT, PET/MRI RMI, SPECT/CT, and scintigraphy;

Pharmacokinetics and pharmacodynamics: pharmaceutical analyses, drug effects, ADME, animal experimentation, and clinical trials;

Pharmaceutical preparations and drug delivery: dosage form design, bioconjugates, prodrugs, formulation, metabolites, nanomaterials, nanomedicines, and drug targeting.

Impact Factor: 4.8 (2024); **5-Year Impact Factor:** 4.9 (2024)



pharmaceutics
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Pharmaceutics (ISSN 1999-4923) is an open access journal which provides an advanced forum for the science and technology of pharmaceuticals and biopharmaceutics. Covered topics include pharmaceutical formulation, process development, drug delivery, pharmacokinetics, biopharmaceutics, pharmacogenetics, and interdisciplinary research involving, but not limited to, engineering, biomedical sciences, and cell biology. Our aim is to encourage scientists to publish their experimental results and theoretical assumptions in as much detail as possible. There is no restriction on the maximum length of the papers. The full experimental details must be provided so that the results can be reproduced. In addition, this journal presents the following unique features:

- Manuscripts regarding research proposals and research ideas will be particularly welcomed
- Computed data or files regarding the full details of the experimental procedures can be deposited as supplementary material if it is not possible to published them in the Material and Methods section, as usual
- We also accept manuscripts addressed to a broader audience, regarding research projects financed by public funds

Impact Factor: 5.5 (2024); 5-Year Impact Factor: 5.8 (2024)

Invited Speakers



Prof. Dr. Patricia Rijo
Lusófona University, Lisbon,
Portugal



Prof. Dr. Christina Lamers
Institute for Drug
Discovery, Faculty of
Medicine, University
Leipzig, Leipzig, Germany



Dr. Darren Fayne
Molecular Design Group,
School of Chemical Sciences,
Dublin City University, Dublin,
Ireland



Dr. Fiora Artusio
Department of Applied
Science and Technology,
Politecnico di Torino, Torino,
Italy



Dr. Carla Serri
Department of Medicine,
Surgery and Pharmacy,
University of Sassari,
Sassari, Italy



Prof. Dr. Ana Catarina da Silva
UCIBIO (Research Unit on
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REQUIMTE (Rede de Química e
Tecnologia), MEDTECH
(Medicines and Healthcare
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**Dr. Ekaterina-Michaela
Tomou**

Section of Pharmacognosy
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Session 1. Opening session

Session 2. Invited lectures

sciforum-154496: The power of cyclic peptides – therapeutic targeting of the complement cascade

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Institute for Drug Discovery, Faculty of Medicine, University Leipzig, Germany

Peptides have traditionally been perceived as poor drug candidates due to unfavorable characteristics mainly regarding their pharmacokinetic behavior, including plasma stability, membrane permeability and circulation half-life. Nonetheless, in recent years, general strategies to tackle those shortcomings have been established, and peptides are subsequently gaining increasing interest as drugs due to their unique ability to combine the advantages of antibodies and small molecules. Macrocyclic peptides are a special focus of drug development efforts due to their ability to address so called ‘undruggable’ targets characterized by large and flat protein surfaces lacking binding pockets. Especially in the field of complement therapeutics this has resulted in two remarkable approvals of cyclic peptides, Pegcetacoplan and Zilucoplan. Both are the first cyclic peptides reaching the market which have been de-novo evolved by display methods.

Our group focuses on the development of cyclic peptides by using chemically modified phage display and computational design, with special emphasis on complement modulation. In a recent project we focused on the complement receptors CR3 and CR4. These members of the $\beta 2$ -integrin family are involved in complement-dependent phagocytosis and leukocyte adhesion, migration, and activation, thereby playing important roles in immune surveillance and inflammation. The direct involvement of $\beta 2$ -integrin receptors in autoimmune, inflammatory, and age-related diseases render them interesting drug targets, however their complex interplay to a multitude of endogenous protein ligands is not well understood. By developing CR3-targeting cyclic peptides, we aim to gain more insights in its ligand binding sites, and to ultimately modulate leukocyte function. Phage display screening against CR3 α MI identified a set of cyclic peptides with direct binding to the α MI domain and able to compete with endogenous ligands. We conducted structure-activity relationship and plasma stability studies and investigated modulating activities in functional adhesion assays.



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sciforum-154766: Influence of Hyaluronic Acid Molecular Weight on Hybrid Nanoparticles for Nasal Silibinin Delivery

Carla Serri ^{1*}, Federica D'Aria ², Miriam Piccioni ³, Gennaro Sanità ⁴, Diana Alister ², Giovanna Rassu ¹, Emanuela Esposito ³, Paolo Giunchedi ¹, Concetta Giancola ², Stefania Crispi ³ and Elisabetta Gavini ¹

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Gliomas, particularly glioblastoma multiforme, are highly aggressive brain tumors characterized by poor prognosis, mainly due to the blood-brain barrier limiting drug delivery. The intranasal route has been identified as a promising strategy for bypassing this barrier. Silibinin (SLB) is a natural flavonoid that inhibits glioma cell growth and invasion while inducing apoptosis, highlighting its potential as a therapeutic agent for glioblastoma. Hyaluronic acid (HA), a naturally occurring glycosaminoglycan, is recognized for its mucoadhesive, biocompatible, and targeting properties, mainly through its interaction with the CD44 receptor and other proteins overexpressed in tumor cells. In this context, HA-based hybrid lipid/polymeric nanoparticles (LPNs) were developed using HA of varying molecular weights for the intranasal delivery of SLB targeted to glioma tumors. Formulations were produced using low-, medium-, and high molecular-weight hyaluronate salts.

LPNs were prepared using a nanoprecipitation method. Physicochemical characterization included measurements of particle size and stability over 30 days, surface charge (ζ p), morphology (via Cryo-TEM), thermal properties (DSC and ITC), total drug content in dispersion (DC), and encapsulation efficiency (EE). Mucoadhesive and viscosity properties were assessed to determine the potential for adhesion to nasal mucosa. In-vitro SLB- release kinetics studies were carried out. Cytotoxicity assays and cellular uptake tests were performed in RPMI 2650 nasal epithelial cells and T98-G glioblastoma cells to evaluate the potential of HA-SLB-loaded LPNs for targeted glioma therapy via intranasal administration.

Blank LPNs had an average size of approximately 100 nm, while SLB-loaded LPNs measured about 160 nm. The LPNs exhibited a negative ζ p around -44.4 mV, indicative of good colloidal stability and confirming the presence of HA on the surface. Cryo-TEM analysis revealed spherical particles with an internal multilayer bilayer structure and a well-defined membrane thickness. ITC and DSC analyses suggested increased stability and an amorphous state of SLB within the LPN matrix, particularly when using low molecular weight HA. The formulations demonstrated good physicochemical stability over 30 days. DC and EE in the dispersions were approximately 100% and 60%, respectively. In-vitro release studies indicated that LPNs achieved a higher SLB release (85%) compared to free SLB (20% in 1 hour), highlighting the influence of low molecular weight HA on nanoparticle performance. The LPNs showed appropriate viscosity and mucoadhesive properties for nasal administration, regardless of HA molecular weight. Cellular uptake studies in RPMI 2650 cells confirmed efficient internalization, while cytotoxicity assays in T98-G glioblastoma cells demonstrated promising therapeutic efficacy through significant glioma cell growth inhibition.

The findings highlight the fundamental role of hyaluronic acid molecular weight in optimizing hybrid nanoparticles (LNPs), demonstrating their strong potential for intranasal delivery of hydrophobic natural compounds to overcome limitations of conventional routes and enhance therapeutic efficacy in glioma treatment.



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sciforum-154751: Phytochemical insights of selected Greek Lamiaceae species

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The Lamiaceae family is among the largest plant families, including more than 230 genera and 7,000 species. Many members of this family are well known for their aromatic and medicinal properties, attributed to their rich content of specialized metabolites. In Greece, the genera *Sideritis*, *Stachys*, and *Salvia* hold particular importance due to their traditional uses and their value as sources of bioactive compounds. This study aimed to investigate the phytochemical composition of selected Greek species belonging to these genera. Plant materials were extracted, and their chemical profiles were analyzed through several analytical techniques. The results revealed a high diversity of polyphenolic compounds, including mainly flavone 7-O-allosylglucosides and phenylethanoid glycosides in *Sideritis* and *Stachys* species, while flavone glycosides and depsides are present in *Salvia* species. Overall, the studied Greek species represent valuable sources of polyphenolic constituents with promising pharmacological activities and potential applications in pharmaceuticals, nutraceuticals, and cosmetic formulations.



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sciforum-154756: Plectranthus-Derived Abietanes: A Natural Source of Drug Candidates

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The genus *Plectranthus*, belonging to the Lamiaceae family, has emerged as a valuable source of bioactive natural products, particularly abietane-type diterpenoids. These compounds, rooted in traditional medicinal practices, have gained attention for their diverse pharmacological properties and potential as drug leads. Abietanes isolated from *Plectranthus* species exhibit a wide range of biological activities, including antimicrobial, anti-inflammatory, and anticancer effects, making them attractive scaffolds for therapeutic development. This presentation highlights the translational journey of *Plectranthus*-derived abietanes from ethnobotanical relevance to preclinical evaluation. Notable examples include Parvifloron D from *P. ecklonii* and 7 α -acetoxy-6 β -hydroxyroyleanone from *P. grandidentatus*, both demonstrating significant bioactivity. A particular focus is placed on dibenzoylroyleanone (RoyBz), a patented abietane diterpenoid with selective activation of protein kinase C (PKC) and potent antiproliferative effects in colon cancer models. Mechanistic studies reveal that RoyBz induces apoptosis via a PKC δ -mediated mitochondrial pathway and disrupts cancer cell metabolism, underscoring its promise as a drug candidate. By integrating phytochemical profiling, pharmacological screening, and molecular investigations, this work reinforces the role of *Plectranthus* species as a rich source of novel therapeutic agents. It also emphasizes the importance of preserving traditional knowledge and validating it through modern scientific approaches to support sustainable drug discovery from natural products.



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sciforum-154759: The crystallization chronicle: solute, protein, solvent

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Crystallization is widely employed in the pharmaceutical industry, ranging from the early stages of drug discovery and formulation to the large-scale production of pharmaceuticals. The process involves the formation of a new crystalline solid phase and can target either a solute, e.g., small molecule or protein, or the solvent, e.g., freezing of water.

The crystallization of solutes assisted by functionalized surfaces will be first discussed. Self-assembled monolayers immobilized on glass can modify the nucleation kinetics of small molecules, i.e., aspirin, and macromolecules. The role of secondary interactions between the surface and the solute was investigated through thin-film crystallization and X-Ray diffraction. Modified surfaces can also promote the formation of unknown polymorphs, thus showing the potential of this technique during the early stages of drug discovery.

The crystallization of proteins will be successively described considering diffusion-dominated environments. The elimination of convection allows better control over crystallization, promotes reproducible crystal size, and reduces the risk of crystal breakage. The use of agarose and silica gels will be presented and their advantages and limitations described, together with strategies to overcome them.

Finally, a focus on solvent crystallization will be provided. Freeze-drying is selected as a case-study as the ice crystals' morphology impacts the freeze-dried product morphology and, consequently, the drying rate, the residual moisture, and the reconstitution time. Freezing of unit doses in vials is a complex process, and the impact of thermal interactions among vials on ice crystallization and final product morphology will be discussed by comparing experimental data and mathematical modelling.



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sciforum-154749: The promise of the nose-to-brain route in drug administration

Ana Catarina da Silva

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The intranasal route has emerged as a promising alternative for the treatment of neurological disorders, owing to its unique advantages, most notably the ability to deliver drugs directly from the nasal cavity to the brain (nose-to-brain delivery). This approach bypasses the blood-brain barrier and can enhance therapeutic efficacy. In recent years, the potential of the nose-to-brain route to improve the management of neurological disorders such as Alzheimer's disease, epilepsy, and migraine has attracted significant preclinical attention. The findings so far are encouraging, particularly when this route is combined with nanosystem-based formulations, including solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC). Nevertheless, evidence supporting the clinical efficacy of the nose-to-brain pathway remains limited, and further research is required before progressing to clinical trials.



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sciforum-154762: Using tiered computational screening to discover small molecule inhibitors of the SARS-CoV-2 NSP3 protein Mac1 domain

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As new medications are used to treat COVID-19, many studies have reported that proteins such as spike, polymerase and proteases are prone to high levels of mutation that can create resistance to therapy over time. Thus, it becomes necessary to, not only target other viral proteins such as the non-structural proteins (NSP's), but to also target the most conserved residues of these proteins. A synergistic combination of bioinformatics, computer-aided drug-design and in-vitro studies can feed into better understanding of SARS-CoV-2 (SC-2) and therefore help in the development of small molecule inhibitors against the NSP's. As part of our initial anti-viral work, a pharmacophore study on NSP15 found a hit molecule (INS316) that made interactions with Ser293, Lys344 and Leu345 residues which are highly conserved across SC-2.

Our group was selected to enter an international challenge organized by CACHE to find inhibitors for the Mac1 domain of SC-2 NSP3. Our MSA alignment results of ~1 million NSP3 sequences indicated that the Mac1 domain is a highly conserved pocket that can be targeted for developing promising SC-2 inhibitors. We used a tiered screening workflow which included the use of volume/shape information of the binding pockets (fastROCS), use of in-house pharmacophore generation software (MoPBS/MOE) and performed docking in the binding pocket (FRED) to rank compounds for subsequent clustering and to identify hits that bind to these conserved pockets. The primary experimental validation results provided by CACHE found that two of our predicted hits show activity in HTRF and SPR assays.



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Session 3. General

sciforum-128072: „New Findings and Developed Analytical Approaches for Visible Spectrophotometric Quantitative Evaluation of Ibuprofen in Three Different Pharmaceuticals”

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Ibuprofen is a propionic acid derivative, non-steroidal drug provided with a very effective anti-inflammatory and analgesic actions and an increased antipyretic effect. The main purpose of this research was to establish and develop an effective spectrophotometric method to exactly quantify and verify the Ibuprofen amount from three different pharmaceuticals, according to the Rules of Good Pharmaceutical Practice provided by the International and European Pharmacopoeias. By spectrophotometric proposed method, Ibuprofen quantitatively reacted with alcoholic α -naphthylamine 0.1 % and sodium nitrite NaNO_2 5%-6%, by heating at 72-73°C for 20 minutes. It was observed the quantitative synthesis of orange azo dye with a pale yellowish tint, dosed in the Visible (VIS) field at $\lambda = 466 \text{ nm}$, in relation to absolute ethanol as a blank. For the first pharmaceutical product, pure Ibuprofen amount determined at $\lambda = 466 \text{ nm}$ was found to be 598.750 mg. This amount found was assigned to a mean percentage content of 99.792 % , provided with average percentage deviation of only 1.958 % , below the officially maximum stated value $\pm 5\%$ and was very close to the officially declared content (600 mg). Regarding the second and third pharmaceuticals, calculated amounts of Ibuprofen were 394,774 mg corresponding to 98,694% Ibuprofen and 197,780 mg assigned to 98,890 % pure Ibuprofen content , respectively. These determined amounts for the second and third products were very close to the officially stated amounts of 400 mg and 200 mg ,and presented average percentage deviations (+) 1.306 % and (+) 1.110 % , both located below the maximum allowed percentage value $\pm 5\%$, officially stated by European and International Pharmacopoeias Rules.



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sciforum-151953: Exploring the Antimicrobial and Anticancer Potentials of 3-Hydrazinoquinoxaline-2-thiol: In vitro and In silico Evaluation

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Background: This study aimed to investigate the in vitro antibacterial, antifungal, anticandidal, and anticancer effects of 3-hydrazinoquinoxaline-2-thiol, as well as its in silico properties. The compound's effectiveness was evaluated against various bacterial strains, fungal species, Candida species, and its potential anticancer effects.

Method: In vitro assays were conducted to evaluate the antibacterial, antifungal, anticandida, and anticancer activities of 3-hydrazinoquinoxaline-2-thiol. Antibacterial activity was tested against both Gram-positive and Gram-negative bacteria, while antifungal and anticandida effects were assessed on various fungal and Candida species. Anticancer activity was evaluated using the MTT assay on multiple cancer cell lines, including breast, colorectal, leukemia, and glioblastoma cell lines. Migration and colony formation assays were also performed. In silico studies investigated the compound's mode of action, safety, and pharmacokinetic properties.

Result: The compound 3-hydrazinoquinoxaline-2-thiol exhibited significant antibacterial activity. Against *E. coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus*, the compound showed mean inhibition zones of 18.33 ± 1.25 mm, 10.5 ± 4.27 mm, and 13.83 ± 4.41 mm, respectively. For filamentous fungi (*Alternaria* sp., *Sclerotinia sclerotiorum*, *Fusarium equiseti*), the compound effectively reduced growth, with mean values of 1.81 ± 0.05 , 2.29 ± 0.04 , and 2.40 ± 0.10 , respectively. Regarding Candida species, *C. albicans*, *C. dubliniensis*, and *C. parapsilosis* demonstrated inhibition with mean values of 1.93 ± 0.29 , 1.68 ± 0.22 , and 0.85 ± 0.17 , respectively. Preliminary anticancer results from the MTT assay indicate potential activity against various cancer cell lines.

Conclusion: 3-Hydrazinoquinoxaline-2-thiol demonstrates potent in vitro antibacterial, antifungal, and anticandidal properties, along with promising anticancer potential. In silico studies further support its therapeutic potential, warranting further exploration for clinical



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sciforum-152006: Multifaceted Evaluation of Anticancer, Antibacterial, Antifungal, and Anti-Candida Properties of Novel Cannabinoid Receptor 2 (CB2R) Ligands: An Integrated In Vitro and In Silico Analysis

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Background: Cannabinoid Receptor 2 (CB2R) is a key target in cancer therapy, with several potential therapeutic applications still to be explored. CB2R ligands, including agonists, antagonists, and inverse agonists, represent a diverse class of compounds with promising effects in various biological contexts. However, their full therapeutic potential remains underexplored. In this study, we investigate the effects of the CB2R agonist CB65 and the inverse agonist JTE907 for antibacterial, antifungal, anti-Candida, and anticancer activities using both in vitro and in silico approaches. **Method:** In vitro assays were conducted to evaluate the antibacterial, antifungal, anti-Candida, and anticancer effects of CB65 and JTE907. Antibacterial activity was assessed against Gram-positive and Gram-negative bacteria. Antifungal and anti-Candida effects were tested on various fungal and Candida species. Anticancer activity was measured using the MTT assay on MDA-MB231 breast cancer cells. Additionally, in silico docking simulations were carried out using Maestro software to investigate the compounds' mechanisms of action. **Result:** Both CB65 and JTE907 showed negligible antibacterial activity against *E. coli*, *K. pneumoniae*, and *S. aureus*. However, both compounds demonstrated significant antifungal activity against filamentous fungi, including *Alternaria* sp., *Sclerotinia sclerotiorum*, and *Fusarium equiseti*. The mean growth inhibition values were 2.61 ± 0.18 , 2.26 ± 0.13 , and 3.15 ± 0.24 for CB65, and 2.90 ± 0.05 , 2.73 ± 0.19 , and 2.64 ± 0.15 for JTE907. Neither compound exhibited anti-Candida activity against *Candida albicans*, *Candida dubliniensis*, or *Candida parapsilosis*. For anticancer activity, CB65 and JTE907 showed IC₅₀ values of 59.38 μ M and 18.23 μ M, respectively, in MDA-MB231 breast cancer cells. In silico docking results supported the experimental data, revealing possible mechanisms of action for both compounds. **Conclusion:** CB65 and JTE907 exhibited significant antifungal activity against filamentous fungi and anticancer potential in MDA-MB231 cells, but showed limited antibacterial and anti-Candida effects. These findings were supported by in silico studies, which suggested underlying mechanisms of action.



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sciforum-151515: Bioanalytical Method Development and Validation for PLC, RCB, and LIT in Human Plasma Using HPLC-UV

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Background:

Accurate and validated bioanalytical methods are essential for drug quantification in biological matrices to support pharmacokinetic and therapeutic drug monitoring studies. Palbociclib, Ribociclib and Letrozole are clinically relevant drugs; however, to date, no simultaneous bioanalytical method has been reported for their estimation in human plasma using HPLC-UV.

Materials and Methods:

A simple and sensitive high-performance liquid chromatography with ultraviolet detection (HPLC-UV) method was developed and validated for simultaneous determination of Palbociclib, Ribociclib and Letrozole in spiked human plasma. Sample preparation was performed using protein precipitation with acetonitrile. Separation was achieved on an Orochemorosil C18 column (250 × 4.6 mm, 5 µm) using a mobile phase of phosphate buffer (pH 3.0, 10 mM) and acetonitrile (60:40, v/v) at a flow rate of 1.0 mL/min. Detection was carried out at 260 nm.

Results:

The method was linear over the ranges of 10–300 ng/mL (Palbociclib), 10–1000 ng/mL (Ribociclib), and 10–600 ng/mL (Letrozole) with correlation coefficients meeting ICH M10 acceptance criteria. Accuracy, precision, recovery, and selectivity were within acceptable limits. Stability studies in plasma and stock solutions confirmed analyte stability under all tested conditions, with negligible degradation observed. The optimized method demonstrated a short chromatographic runtime and simple sample preparation, enabling rapid analysis of multiple samples.

Conclusion:

The validated HPLC-UV method is simple, precise, and robust. It offers the first reported simultaneous quantification of Palbociclib, Ribociclib and Letrozole in human plasma and is suitable for pharmacokinetic studies, bioequivalence testing, and therapeutic drug monitoring in clinical trials



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sciforum-151553: Cytotoxicity and DNA Damage Biomarkers in the Assessment of Photogenotoxicity

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Phototoxic reactions are of particular concern for pharmaceuticals, cosmetics, and other consumer products that absorb UV-visible light, as they can result in skin damage and increased cancer risk. Current in vitro strategies, such as the 3T3 Neutral Red Uptake and reconstructed human epidermis assays, mainly address photocytotoxicity but fail to capture light-induced DNA damage (photogenotoxicity), a key endpoint for long-term health effects. To overcome these limitations, we developed an in vitro alkaline comet assay in HaCaT human keratinocytes, focusing on biomarkers of light-induced DNA damage (photogenotoxicity). Cytotoxicity was monitored through MTT and LDH assays, while DNA strand breaks served as a biomarker of genotoxic stress. Six reference chemicals (sodium dodecyl sulfate, chlorpromazine, benzophenone-3, 8-methoxypsoralen -8-MOP-, p-phenylenediamine, and 6-methylcoumarin - 6-MC-) were tested. Following UV-A irradiation (4 J/cm²), photocytotoxicity was quantified using Photo-Irritation Factor (PIF) and Mean Photo Effect (MPE) values, while genotoxic effects were determined by the comet assay at immediate and 24 h post-exposure. Phototoxicity was evident for benzophenone-3, 8-MOP, 6-MC and chlorpromazine, reflected in elevated PIF/MPE values. DNA damage, as detected by comet assay, was significant for benzophenone-3, p-phenylenediamine, and chlorpromazine, but absent for 8-MOP, consistent with its DNA crosslinking properties. Importantly, no persistence of DNA strand breaks was observed after 24 h, indicating DNA repair biomarkers of recovery. Altogether, cytotoxicity and genotoxicity biomarkers identified in this study highlight the alkaline comet assay as a relevant tool to detect photogenotoxic hazards in vitro.

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sciforum-121961: Microfluidics-based synthesized ZIF-8 nanoparticles embedded inside a natural scaffold for sustained-release of cargo in drug delivery purposes

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Introduction: The growing field of nanotechnology requires the use of scalable devices such as microfluidic-based channels. These reproducible setups ensure time and labor-saving methods for nanoparticle synthesis. Synthesis of porous ZIF-8 nanoparticles can result in better loading and more controlled release, as well as pH-responsiveness, which are important in cancers and inflammatory diseases alike. Embedding the drug-loaded nanomaterials inside a natural scaffold such as wood adds to the mechanical and controlled-release effects needed in multiple drug delivery aspects.

Methods: The synthesis of drug@ZIF-8 nanoparticles was facilitated through microfluidic tubes. Five different flow rate combinations, 2 different solvents, and 2 different ligand/metal molar ratios were chosen based on the literature in order to reach the optimal size and polydispersity index (PDI) for ZIF-8 nanoparticles. Characterization of the drug/ZIF-8/wood scaffold was performed using scanning electron microscopy (SEM), Fourier-transform infrared spectroscopy (FTIR), and X-ray diffraction (XRD) to assess its structural integrity. Loading and release tests were also conducted.

Results: Morphology and characterization results were assessed. SEM showed a uniform rhombic dodecahedron structure, presenting successful ZIF-8 synthesis with low PDI and less than 200 nm size. Loading capacity (LC%) was 11.68%, with encapsulation efficiency (EE%) of around 76%. The release of statin from ZIF-8 nanoparticles was evaluated in phosphate-buffered saline (PBS) with 2 pH values, revealing a burst profile, while a sustained release profile was observed from the scaffold, taking two months to reach full release. pH-responsive behavior was observed, which is beneficial for drug delivery towards inflamed areas.

Conclusion: This study presents the construction and evaluation of a novel wood-based scaffold integrated with microfluidics-synthesized ZIF-8 nanoparticles aimed at promoting drug delivery aspects such as loading and release profile.

The scaffold represents a promising strategy for tissue regeneration, a field that may benefit from slow and pH-triggered release for better outcomes.



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sciforum-151497: MMP-1 and IL-6: novel biomarkers to identify phototoxic chemicals

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Photoallergy can be considered a special type of contact hypersensitivity, in which UV light activates the allergen and, therefore, the physiological mechanisms involved in the development of symptoms. In the case of pharmaceuticals, preclinical trials should include phototoxicity and photoallergy assays to ensure their safety. However, nowadays there is still a lack of non-animal methods to predict potential photoallergic reactions. Knowledge of the pathophysiological mechanisms of photoallergic contact dermatitis at different levels, such as molecular and cellular ones, is thus an important field of research. In this sense, this work explores the use of a cell line of skin keratinocytes to develop a vitro assay to identify phototoxic molecules and discriminate between photirritant and photoallergic by differential secretion of humoral molecules. To achieve this goal, keratinocytes have been exposed to different chemicals at various concentrations with well-known phototoxic potential concomitantly with 4 J/cm² UVA or maintained in dark. The chemicals assayed were Chlorpromazine (photoirritant and photoallergen); 8-methoxypsoralen (photoirritant); Benzophenone (photoallergen) and *p*-phenilendyamine (allergen). After 24 hours post-incubation cell viability was determined and the concentration that induces an 80% of cell viability in dark and UVA conditions was calculated. Then, the secretion of different metalloproteinases (10) and inflammatory cytokines (40) in supernatant was evaluated by semi-quantitative arrays (RayBiotech). Our results indicate that MMP-1 and IL-6 are potential biomarkers to discriminate between photoirritant and photoallergic reactions. Next step includes to evaluate the release of both biomarkers with a more quantitatively assay as ELISA and increasing the number of chemicals studied.

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sciforum-151055: mRNA delivery significantly improves the efficiency of VSV-based cancer immunotherapy

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Introduction. Oncolytic viruses (OV), a novel class of anti-cancer therapies, selectively replicate in cancer cells and activate the immune response. The unique OV-targeted destruction of malignant cells sets OV-based therapies apart from the non-specific conventional chemo-, radio-, and even targeted antibody-based therapies. However, the sensitivity of cancer cell lines to rVSV and, hence, the success of virotherapy, may differ depending on cancer type and the strength of the anti-viral response. At the same time, the oncolytic potency of rVSV decreases as a result of the insertion of larger genes (such as interleukin-12, IL12, and granulocyte macrophage colony-stimulating factor, GM-CSF, used to potentially activate the dampened immune response) into the viral genome as compared to green fluorescent protein (GFP). Therefore, the combination of rVSV and mRNA-delivered immunostimulatory factors may increase the efficiency of anti-tumor therapy.

Methods. rVSV-mIL12-mGM-CSF cytotoxicity was assessed in vitro on three murine cancer cell lines: B16-F10, LL/2, and CT26 24 hours post-infection by flow cytometry. In vivo experiments were performed on syngeneic models via intratumoral injection of rVSV. Quantitative PCR (qPCR) analysis was performed to assess the mRNA expression levels 12 hours post-infection in vitro.

Results. Based on the obtained data, Lewis lung carcinoma (LL/2) cells were more susceptible to oncolysis compared to colon carcinoma (CT26) or melanoma (B16-F10). Detection of expression levels of certain antiviral and pro-apoptotic genes in response to the rVSV infection by qPCR showed higher levels of IFN β and p53 and lower levels of IFIT, RIG-I, and N-cadherin in LL/2 cells. Subsequently, C57BL/6 and BALB/c mice, infused subcutaneously with B16-F10 and LL/2 cells, respectively, were injected intratumorally with rVSV-mIL12-mGM-CSF to assess the synergistic effect of rVSV and immunostimulatory factors. The in vivo study demonstrated tumor growth inhibition (TGI) of over 50% for both cancer models. Finally, we assessed the combined effect of two platforms: mRNA-LNP-based delivery of mIL-12 and mGM-CSF and rVSV-mediated oncolysis, leading to TGI of 95% in animals with colon cancer.

Conclusions. The unique combination therapy approach significantly improved therapy outcome. These promising results are giving hope that this novel approach will also be successful for melanoma and lung carcinoma models in the near future.



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sciforum-152292: Photosensitizer-Enhanced Radiotherapy Reduces Giant Cancer Cell Formation in HeLa and A431 Models

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Giant cancer cells are abnormal tumor cells that often arise after ionizing radiation (IR) treatment. Their persistence is associated with tumor resistance, recurrence, and poor clinical outcomes, highlighting the need for strategies that can eliminate them effectively. Radiotherapy (RT), which uses IR to damage tumor DNA, remains an indispensable method of choice in cancer therapy. Photodynamic therapy (PDT), by contrast, involves a photosensitizing drug and light activation to produce reactive oxygen species (ROS) that destroy cancer cells. Importantly, photosensitizers may also act as radiosensitizers, making them promising candidates for combination therapy.

In our study, we tested whether combining PDT and RT could improve cancer cell killing and reduce giant cell formation. HeLa (cervical carcinoma) and A431 (epidermoid carcinoma) cells were treated with Photosens (NIOPIK, Russia), followed by light exposure at 20 J/cm². IR was delivered using a Novalis TX electron accelerator at 600 Gy/hour, with doses guided by the LD50 for both HeLa and A431 cancer cell line (6 Gy).

The combined treatment showed a strong cytotoxic effect and, importantly, caused a marked reduction in the proportion of giant cancer cells formed compared to IR alone. Our results suggest that combining PDT with RT provides a dual attack strategy that not only improves tumor cell killing but also reduces the formation of giant cells, which may translate into more effective and durable cancer control in clinical practice.

The study was supported by the Ministry of Education and Science of the Russian Federation (State assignment FSWR-2023-0032).



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sciforum-152318: Selenotetrazole Derivatives as Selective Antioxidants with Redox-Modulating Potential

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Oxidative stress plays a central role in the pathogenesis of neurodegenerative, cardiovascular, and inflammatory disorders, as well as cancer. In this sense, the discovery of novel antioxidant agents has a critical priority in medicinal chemistry. Organoselenium derivatives stand out in this context for their ability to modulate redox processes, frequently mimicking the activity of glutathione peroxidase (GPx). At the same time, the tetrazole nucleus functions as a bioisosteric moiety, widely employed in clinically approved drugs due to its favorable pharmacokinetic and pharmacodynamic properties. The strategic combination of these two pharmacophoric elements results in selenotetrazoles, molecules with promising biological potential and new perspectives for therapeutic development. The compounds were obtained via [3+2] cycloaddition between SeCN-containing precursors and sodium azide. In this work, the antioxidant activity of the newly synthesized selenotetrazoles was evaluated through radical scavenging assays (ABTS•+ and DPPH•) to investigate their redox-modulating potential. In the ABTS•+ assay, which measures the ability of molecules to neutralize radicals in aqueous medium, ethyl 3-(1H-tetrazol-5-yl)selenyl benzoate and ethyl 4-(1H-tetrazol-5-yl)selenyl benzoate at 200 µM showed significant antioxidant activity, comparable to ascorbic acid (positive control, 25 µM). Conversely, in the DPPH• assay, which evaluates electron transfer in apolar medium, the compounds showed no significant activity. This selectivity suggests that their antioxidant effect is not based on electron transfer in nonpolar systems, but rather occurs in aqueous environments, consistent with a GPx-like mechanism. In conclusion, the synthesized selenotetrazoles present selective antioxidant activity, redox stability and multitarget potential, consolidating them as promising scaffolds for the development of antioxidant, anti-inflammatory, neuroprotective and/or anticancer agents.



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sciforum-152029: The effect of oligonucleotides, mononucleotides and their complexes with mannitol on the conformational stability of Interferon $\alpha 2b$

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The study aimed to comprehensively investigate the effect of various forms of oligonucleotides (ORNs) (acidic, salt, and complexes with mannitol) and mononucleotides on the conformational stability and aggregation properties of interferon $\alpha 2b$ (IFN $\alpha 2b$), a key protein in the antiviral response.

Circular dichroism (CD) was used to analyse the secondary structure of the protein, and fluorescence spectroscopy with thioflavin T was used to assess its tendency to aggregate. CD spectroscopy data clearly demonstrated that protein concentration significantly affects the results of the analysis. At a low concentration of 0.6 mM, the α -helix content was higher (up to 18.4%) than in 1.6 mM IFN $\alpha 2b$ samples, where it did not exceed 4.2%. Importantly, during six months of observation with 6 freeze-thaw cycles, no statistically significant changes in the secondary structure of the protein were detected for any of the concentrations, indicating no degradation or significant conformational change of IFN $\alpha 2b$ over time.

To assess thermal stability, thermal denaturation experiments were performed. It was found that the addition of the studied ligands (ORN and their complexes with mannitol) leads to an increase in the melting temperature (T_m) of the protein from 62 °C to 63.8–64 °C, indicating a slight stabilising effect. This confirms the binding of ligands to the protein and their impact on its conformational state. In addition, fluorescence studies with thioflavin T did not reveal any signs of pathological amyloid aggregate formation under the influence of any of the studied compounds.

Thus, the results of the study indicate that oligonucleotides and their complexes do not cause destabilisation or harmful aggregation of interferon $\alpha 2b$, but rather demonstrate a moderate stabilising effect. The data obtained confirm the potential safety and compatibility of such compounds with protein therapeutics, which may be important for the development of new combined immunomodulatory and antiviral drugs.



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Session 4. New Small molecules as drug candidates

sciforum-152370: Synthesis and Cytotoxicity Profiling of Pyridine-Based Melanostatin Peptidomimetics Targeting Parkinson's Disease

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Parkinson's disease (PD) is the second most prevalent neurodegenerative disorder of central nervous system (CNS), characterized by the progressive loss of mesencephalic dopaminergic neurons. Current therapies provide symptomatic relief but do not halt disease progression, highlighting the urgent need for novel and innovative therapeutic strategies.

Melanostatin (MIF-1), a hypothalamic neuropeptide and positive allosteric modulator (PAM) of dopamine D2 receptors, has emerged a promising candidate for PD treatment. However, its peptide nature restricts clinical use due to its poor oral bioavailability and limited metabolic stability.

In this work, we designed and synthesized twelve novel analogs using pyridine-based carboxylic acids as prolyl surrogates to address the pharmacokinetic limitations of MIF-1. Pyridine-based scaffolds are known for their structural versatility and CNS drug-like properties, including neuroprotective and neurotransmitter-modulating effects.

Structure-cytotoxicity relationship studies in differentiated SH-SY5Y cells identified that, in this group of analogs, the methyl ester group acts as a toxicophore, whereas the corresponding amide counterparts exhibited improved toxicological profiles. These findings offer valuable insights for the development of novel pyridine-based MIF-1 analogs with adequate toxicological profiles.

The analogs identified in this preliminary study are suitable to undergo pharmacological functional assays to characterize PAM activity, contributing to the development of safer and more effective anti-Parkinson agents.



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***sciforum-152185: In silico* elucidation of the binding affinity of puerarin and adenine with tight junctional proteins (ZO-1, Occludin, and claudin 4) to restore gut barrier integrity**

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Over the past two decades, gut dysbiosis has gained significant attention due to its multifaceted involvement in diverse health disorders. Gut barrier dysfunction increases intestinal permeability, which allows gut-derived toxicants into the systemic circulation and contributes to adverse health outcomes. The proteins, including zona occludens 1 (ZO-1), occludin, and claudin 4, maintain the integrity through forming a tight junction complex and restricting the entrance of noxious substances through the intestinal epithelial apical layer. It had been reported that the reduction in the relative expression of mucosal junctional proteins can trigger a broad spectrum of disorders, including inflammatory bowel diseases, renal impairment, neurocognitive dysfunctions, autoimmune disorders, colorectal cancer, and others. Preclinical studies demonstrate the role of puerarin in restoring the intestinal barrier function through increasing the levels of tight junction proteins and exerting anti-inflammatory and antioxidant effects. Furthermore, previous scientific evidence suggested the deteriorating effects of higher concentrations of adenine on the intestinal barrier functions. This study aims to elucidate the molecular docking of puerarin and adenine against the ZO-1, occludin, and claudin 4. Puerarin shows a lesser binding energy against ZO-1 (−7.187 kcal/mol) and claudin 4 (−9.193 kcal/mol), whereas no significant results were obtained in the case of occludin. They exhibit stronger hydrophobic interaction and hydrogen bonding to the amino acid residues present at the active site of the ZO-1 and claudin 4. In contrast, adenine displayed fewer interactions, likely due to its inhibitory effects at the active site pockets of ZO-1, occludin, and claudin 4. These findings suggest that puerarin may have therapeutic potential in modulating tight junctional proteins. However, further *in vitro* and *in vivo studies* are required to determine the preventive effects against gut dysbiosis-associated health complications and intestinal disorders.



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sciforum-150831: Design, Synthesis, and Biological Evaluation of Novel Sigma Receptor Ligands Based on 4-Amino Piperidine Scaffolds

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Sigma receptors (σ_1 and σ_2) are non-opioid chaperone proteins localized at the mitochondria-associated membranes of the endoplasmic reticulum, where they regulate calcium signaling, protein homeostasis, and cell survival. They have emerged as attractive therapeutic targets in cancer, neurodegeneration, addiction, and pain. However, the discovery of selective sigma receptor ligands remains challenging due to overlapping structural requirements and limited scaffold diversity. In this study, we investigated 4-amino piperidine derivatives as a promising framework for the development of novel sigma receptor ligands.

A focused library of 4-amino piperidine-based compounds was synthesized, and their chemical identity and purity were confirmed by LC-MS, $^1\text{H}/^{13}\text{C}$ NMR spectroscopy, and melting point analysis. Systematic modifications were introduced at the 4-amino position and the piperidine nitrogen, incorporating electron-donating, electron-withdrawing, and hydrophobic substituents to assess their influence on sigma receptor binding. Preliminary binding affinity studies were performed through the National Institute of Mental Health Psychoactive Drug Screening Program (NIMH PDSP, UNC), where several compounds demonstrated significant inhibition at sigma receptors while exhibiting minimal off-target activity across a panel of CNS receptors.

Overall, this work highlights the potential of 4-amino piperidine derivatives as novel sigma receptor ligands. Ongoing efforts aim to optimize affinity and selectivity, thereby advancing their translational potential in therapeutic areas involving sigma receptor modulation.



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sciforum-125055: *Paeonia lactiflora* root extract as a promising phytochemical for LPS-induced skin inflammation management

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Skin inflammation is a protective biological response to tissue damage, mediated by various inflammatory factors. Notably, transient receptor potential vanilloid (TRPV) channels have been implicated in this process, which involves dysregulation of both immune and non-immune cells. As such, targeting TRPV1 has emerged as a promising therapeutic strategy for inflammatory skin conditions.

Paeonia lactiflora Pall., a rich source of bioactive compounds such as the terpene glycoside paeoniflorin, exhibits notable antioxidant and analgesic properties. This study investigated the effects of *Paeonia lactiflora* root extract standardized for paeoniflorin on LPS-induced inflammation in skin keratinocytes using *in silico* and *in vitro* approaches.

Molecular docking simulations predicted paeoniflorin's binding affinity for the TRPV1 transmembrane domain. *In vitro* research results demonstrated significant dose-dependent anti-inflammatory effects of the extract on HaCaT keratinocytes. At a concentration of 0.05 mg/mL, the extract showed remarkable efficacy, reducing excessive TNF- α levels by 148.82%, IL-6 by 37.78%, and IL-13 by 68.63% compared to difference between LPS and basal controls (p0.01). The analgesic effect may be linked to TRPV1 channel amount decrease by 113.47% to difference between LPS and basal controls (p0.01).

These results confirm the *Paeonia lactiflora* extract has dual pharmacological potential for inflammatory skin conditions through cytokine and TRPV1 modulation. These findings highlight the therapeutic prospectives of *Paeonia lactiflora* extract for alleviation of skin inflammation.



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sciforum-152036: Synthesis and Evaluation of Anti-Proliferative Potential of 2-((2-chloroquinolin-3-yl)methylene)-3,4-dihydronaphthalen-1(2H)-ones in Breast Cancer

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Abstract:

The highly dynamic microtubules of the mitotic spindle are well-established biochemical targets for anticancer drugs such as paclitaxel, vinblastine, and vincristine. However, a significant clinical challenge is the emergence of resistance to these agents, highlighting the urgent need for novel anticancer compounds that target tubulin. In this study, a panel of chloroquinoline derivatives was synthesized and characterized using ¹H NMR, FTIR, and mass spectrometry. The antiproliferative activity of these compounds was evaluated against the breast cancer cell lines MCF-7 and MDA-MB-231. Of the tested molecules, CQ-9 and CQ-14 displayed IC₅₀ values of 5.6 μM and 4.55 μM, respectively, against MDA-MB-231 cells, while CQ-9 exhibited an IC₅₀ of 13.05 μM for MCF-7 cells. All compounds (CQ-1 to CQ-14) were subjected to molecular docking studies using the Schrödinger software suite to investigate their interactions with tubulin. The resulting ligand-protein complexes were analyzed for binding energies, and the most stable complexes were selected for further molecular dynamics simulations. Tubulin was chosen as a likely target owing to the structural similarity of the reported compounds to quinoliny and other heteroaryl chalcones that have shown to inhibit Tubulin by binding to Colchicine binding site. Hence, we used specific crystal structure of tubulin (PDB id: 1SA0) co-complexed with Colchicine for our molecular docking studies.



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sciforum-150788: Intranasal administration of recombinant chaperone GRP78 is a promising disease-modifying treatment approach for Parkinson's disease and sleep restriction-associated neurodegeneration

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Introduction:

Parkinson's disease (PD) is a neurodegenerative disorder that to date remains incurable. PD is currently linked to chronic sleep restriction (SR) as these pathologies share a similar spectrum of molecular and cellular malfunctions: accumulation of aberrant proteins, neurodegeneration, neuroinflammation, activation of unfolded protein response (UPR) apoptotic branch. Development of neuroprotective strategies for PD and SR-associated neurodegeneration remains a critical issue for pharmaceuticals. Prospective drug candidates should possess high bioavailability for the brain, and the ability to influence main pathogenetic mechanisms of neurodegeneration. One of the promising drug molecules is the GRP78 (HSPA5). The objective of this study was to evaluate the protective potential of recombinant GRP78 (rGRP78) administered intranasally in a PD and SR rodent models.

Methods:

The work was carried out on male Wistar rats (6 months). Microinjections of the proteasome inhibitor lactacystin (LC) into substantia nigra (SN) were used to create a PD model. SR was carried out in a polyphase manner for 5 days using a swinging platform. rGRP78 was administered intranasally 4 and 24 hours after each LC microinjection and every day during SR. Control group received LC and/or GRP78 solvents. Pathomorphological and neurochemical changes were assessed by immunohistochemistry and by Western Blot. Confocal microscopy was used to assess rGRP78 bioavailability. Statistical analysis was conducted via two-factor ANOVA and Tukey post-hoc.

Results:

It was proven that SR and PD share common molecular and cellular pathological mechanisms involved in neurodegeneration. It was established that intranasally administered rGRP78 is internalized by neurons and microglia in various brain structures. rGRP78 prevents development of neurodegeneration in PD and SR due to its ability to counteract (1) α S pathology; (2) apoptotic UPR branch activation; (3) microgliosis and NF- κ B-induced proinflammatory changes.

Conclusion:

rGRP78 is a bioavailable to the brain tissue drug that possesses a complex protective effect in neurodegenerative pathologies.



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sciforum-152374: Characterization of the cytotoxic activity of naphthoxyacetamide hydrochlorides in the A549 lung adenocarcinoma cell line

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Introduction:

Non-small cell lung cancer (NSCLC) is the leading cause of cancer-related mortality worldwide in both men and women. Current therapeutic options rarely achieve complete remission, highlighting the urgent need for new treatments. The sigma-1 (σ_1) receptor has emerged as a promising target since it is overexpressed in several tumor types. Antagonists of this receptor have been shown to inhibit cell proliferation by inducing endoplasmic reticulum stress and promoting the generation of reactive oxygen species. Interestingly, although σ_1 receptors are also present in normal cells, their antagonists selectively trigger cytotoxic effects in cancer cells.

Methods:

In this study, we evaluated the cytotoxic activity of naphthoxyacetamide hydrochlorides through cell viability assays based on the metabolic reduction of MTT. Two compounds were tested: *N*-(2-morpholinoethyl)-2-(naphthalen-2-yloxy)acetamide (salt 1) and *N*-(2-(piperidin-1-yl)ethyl)-2-(naphthalen-2-yloxy)acetamide (salt 2). A549 lung adenocarcinoma cells were seeded at a density of 5000 cells/well in 96-well plates and exposed to different concentrations (0.1–3.16 $\mu\text{mol/mL}$) for 24 h. Absorbance was measured at 575 nm using a microplate reader.

Results:

Salt 2 exhibited a half-maximal inhibitory concentration (IC_{50}) of 0.381 $\mu\text{mol/mL}$, which was comparable to the reference drug cisplatin (0.358 $\mu\text{mol/mL}$). In contrast, salt 1 showed a higher IC_{50} value of 1.419 $\mu\text{mol/mL}$, indicating lower potency.

Conclusions:

Both compounds demonstrated cytotoxic activity against A549 cells, with salt 2 displaying a stronger effect like cisplatin. These findings suggest that salt 2 could be considered a promising candidate for further development as an anticancer agent targeting NSCLC.



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sciforum-150836: Cu(II) and Zn(II) complexes of salen-type Schiff base ligands as promising anticancer agents in treatment of colorectal adenocarcinoma

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Despite significant progress in medicine, cancer continues to be one of the leading causes of death worldwide. Since the discovery of cisplatin's antitumor activity, it has remained one of the most commonly used chemotherapeutics in cancer treatment (1). However, serious side effects of platinum-based drugs significantly limit their clinical use. The study of transition metal complexes and their biological properties (e.g. antimicrobial, cytotoxic, anti-inflammatory, interactions with DNA) are the subject of intensive studies (2). Copper and zinc complexes, as an alternative to platinum-based drugs, display notable anticancer activity while causing fewer side effects than cisplatin. The variation in their biological activity is associated with the molecular structure of the ligand, and the type of central metal ion. Complexes of the salen-type ligands represent a promising group of compounds in medical research. Since colorectal cancer is the third most diagnosed type of cancer, the aim of this work was to prepare and study the antitumor effect of Schiff base ligands derived from 1,2-cyclohexanediamine and fluorine-substituted benzaldehydes and their Cu(II) and Zn(II) complexes (3,4). All derivatives were examined for their antitumor activity against two model human colorectal adenocarcinoma cell lines (HT-29 and Caco-2) by MTT assay. Experimental results showed that in comparison with cisplatin, the studied Cu(II) and Zn(II) complexes can significantly inhibit the growth of both HT-29 and Caco-2 tumor cells. Due to their marked cytotoxic effect, these metal complexes represent a promising alternative for the development of new anticancer agents.

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sciforum-148777: Design, synthesis, and biological evaluation of triazole-linked lignan-monoterpenoid based hybrid molecules as xanthine oxidase inhibitors with potent in vivo efficacy

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A novel series of triazole-linked monoterpenoid-lignan based molecules was designed by employing a molecular hybridization strategy inspired by the pharmacophoric properties of eugenol (monoterpenoid) and its derivatives, and sesamol (lignan). Designed molecules were synthesised and evaluated for their xanthine oxidase inhibitory potential. Among the series of hybrid molecules, MT7 (isoeugenol-sesamol hybrid) showed the most potent xanthine oxidase inhibition ($IC_{50} = 0.263 \mu M$) with a mixed-type of inhibitory pattern and scavenging reactive oxygen species in RAW 264.7 macrophage cells. Furthermore, higher cytotoxic potential of MT7 against xanthine oxidase harbouring cancer cells over non-harbouring cells (A547 skin cancer cells) and reduction in antioxidant enzymes confirms the binding pattern of MT-7 in Mo-cofactor (molybdenum cofactor) binding site. Molecular docking and simulations studies confirmed the stability and favourable interactions of MT7 with the febuxostat binding site of xanthine oxidase. MT7 was non-toxic to mouse fibroblast cells (L929) and showed stability with plasma and liver microsomes. MT7 further emerged as safer for in vivo preclinical investigations in rodent models with an LD_{50} value of 300 mg/kg and showed dose dose-dependent reduction in serum uric acid in potassium oxonate oxonate-induced hyperuricaemia rat model. Overall, studies representing MT7 as high a highly efficaciously efficacy lead for further xanthine oxidase drug development initiatives, and a preclinical candidate with tolerable safety profiles for management of hyperuricemia via xanthine oxidase inhibition.



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sciforum-151419: Evaluation of Anticancer Activity of Pyruvamide 4-Allylthiosemicarbazones and Their Copper(II) Complexes Against the Leukemia THP-1 Cell Line

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According to recent data from the WHO and the International Agency for Research on Cancer, cancer remains one of the leading public health challenges worldwide. Projections suggest that, due to demographic factors such as population growth and aging, the annual number of new cases could reach around 35 million by 2050. The WHO report also highlights that while progress has been made in prevention and treatment, access to effective diagnostic and therapeutic options remains uneven across different regions, particularly in low- and middle-income countries. Leukemia represents a significant cause of cancer-related morbidity and mortality, and the THP-1 cell line, derived from human acute monocytic leukemia, is frequently used as an established *in vitro* model to evaluate the anticancer potential of new compounds. Thiosemicarbazones and their metal complexes are compounds that have long been recognized in the literature as biological agents, including those with anticancer properties.

Based on the above, for our study we synthesized a series of 4-allylthiosemicarbazones of pyruvamides: 1-(piperidin-1-yl)propane-1,2-dione 4-allylthiosemicarbazone (HL¹), 3-(morpholin-4-yl)propane-2,3-dione 4-allylthiosemicarbazone (HL²), and *N*-(4-methoxyphenyl)-2-oxopropanamide 4-allylthiosemicarbazone (HL³), along with their copper(II) chloride complexes [Cu(L¹⁻³)Cl]. The physicochemical properties of all synthesized compounds were investigated to confirm their structure and composition.

The anticancer activity of the synthesized compounds was evaluated against the THP-1 cell line. All copper(II) complexes exhibited higher activity than the corresponding thiosemicarbazones from which they were obtained. HL¹ and HL³ showed no activity, while only 3-(morpholin-4-yl)propane-2,3-dione 4-allylthiosemicarbazone demonstrated activity with an IC₅₀ value of 2.8 µM. The most active compound was [Cu(L²)Cl], with an activity value of 0.14 µM, which is 2.2 times higher than that of Doxorubicin, used as a reference standard in this study.

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sciforum-152305: Fiscalin-Based Compounds as Multifunctional Agents Against Alzheimer's Pathology: Addressing Amyloid Toxicity, Iron Overload, and Cholinergic Deficits

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Alzheimer's disease (AD) is the predominant form of age-related dementia and a major neurodegenerative disorder. Its progression is associated with multiple pathological processes, including amyloid-beta ($A\beta$) deposition, Tau hyperphosphorylation, iron accumulation, mitochondrial dysfunction, and heightened oxidative stress, among other contributing factors [1]. The decline in acetylcholine (ACh) levels due to cholinergic neuron loss further contributes to the cognitive and memory impairments characteristic of AD [2]. With AD cases projected to more than triple by 2050 due to aging populations, and therapeutic options still limited [3], the search for new treatments that directly target these pathological mechanisms is critical. In this context, fiscalins, a class of valine-derived alkaloids with an indolyl moiety and a tricyclic anthranilic acid core, have shown neuroprotective, anticancer, and antimicrobial activities, highlighting their potential therapeutic relevance in AD [4].

This study investigated the *in vitro* cytotoxicity, neuroprotective potential, and acetylcholinesterase (AChE) inhibitory activity of six synthetic fiscalin derivatives using SH-SY5Y cells differentiated into a cholinergic phenotype. Cytotoxicity was assessed after 24 h of exposure to the compounds (0–50 μ M) using the neutral red uptake and MTT reduction assays to define non-cytotoxic concentrations. Neuroprotection against $A\beta$ (50 μ M)- and iron(III) (500 or 1000 μ M)-induced cytotoxicity was subsequently evaluated following 24 h of co-incubation with the derivatives (10 and 25 μ M). Additionally, AChE inhibition was determined using the Ellman's method.

None of the tested fiscalin derivatives exhibited cytotoxicity at concentrations up to 25 μ M. Notably, three compounds significantly reduced $A\beta$ -induced cell death, while five mitigated iron(III)-mediated cytotoxicity. Additionally, five derivatives significantly inhibited AChE activity. Taken together, these findings indicate that fiscalin-based compounds exert multitarget neuroprotective effects relevant to AD pathology, although further studies are needed to elucidate their underlying mechanisms.



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sciforum-152354: Integrated Study of Novel Triazole-Linked Schiff Bases: From Efficient Synthesis and Structural Elucidation to Antimicrobial Activity, DFT, and Molecular Docking

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Introduction:

Triazole-based Schiff bases and their metal complexes have attracted considerable attention due to their potential as therapeutic agents with antimicrobial and anti-inflammatory activities. The present study focuses on the synthesis, characterization, and biological evaluation of novel triazole-linked Schiff bases and their Co(II), Ni(II), and Cu(II) complexes.

Methods:

Two Schiff base ligands (L1 and L2) and their complexes (3–10) were synthesized and structurally characterized. Antimicrobial activity was assessed in vitro against Gram-positive and Gram-negative bacteria (*Staphylococcus aureus*, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Escherichia coli*) and fungal strains (*Candida albicans* and *Cryptococcus neoformans*). Growth inhibition was quantified spectrophotometrically (OD600 for bacteria, OD530 for *C. albicans*, and OD600–570 following resazurin reduction for *C. neoformans*). Anti-inflammatory activity was evaluated using the protein denaturation inhibition assay. Computational studies included density functional theory (DFT), molecular electrostatic potential (MESP) mapping, ADMET predictions, and molecular docking targeting enoyl-acyl carrier protein reductase (*Mycobacterium tuberculosis*, PDB ID: 6H53) and cyclooxygenase-2 (COX-2, PDB ID: 1CX2).

Results:

Ligand L1 displayed remarkable anti-TB potency (MIC: 0.007 ± 0.002 $\mu\text{mol/mL}$), surpassing streptomycin. Among the synthesized complexes, compound (10) was the most potent, showing strong antibacterial and antifungal effects (MIC: 0.0066 $\mu\text{mol/mL}$) and the highest anti-inflammatory activity ($\text{IC}_{50} = 6.75 \pm 0.09$ μM). Docking results supported the experimental findings, with favorable binding energies for both 6H53 and COX-2.

Conclusions:

This integrated experimental and in silico investigation demonstrates that triazole-linked Schiff bases and their metal complexes, particularly complex (10), exhibit significant antimicrobial and anti-inflammatory potential. These findings highlight their promise as lead compounds for the development of future therapeutic agents.



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sciforum-148652: Photodynamic inactivation of *Candida albicans* in different growth forms mediated by BODIPY derivatives

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Candida albicans is an opportunistic fungal pathogen that normally exists as a commensal on human skin and mucosal surfaces, but under certain conditions it can develop virulence factors and exhibit antifungal resistance. Photodynamic inactivation (PDI) has emerged as a promising non-conventional approach to control this microorganism. In this study, the PDI activity of two BODIPY derivatives: a compound bearing a dimethylaminopropoxy group attached to a phenylene unit (BDP 1) and its dibrominated analogue (BDP 2) were evaluated against *C. albicans* in different growth forms. In planktonic cultures, 5.0 μM BDP 1 completely inactivated 1×10^6 and 1×10^7 CFU/mL after 30 min of white light irradiation (90 mW/cm²). The same effect was achieved with only 0.25 μM BDP 2 after an irradiation of 15 min. Additionally, a ~ 2 log reduction was observed in cultures containing 1×10^8 CFU/mL treated with 5.0 μM BDP 2 and 30 min of irradiation. Mechanistic assays revealed that BDP 1 mainly acts via type I photoprocesses, while BDP 2 predominantly generates singlet molecular oxygen. In pseudohyphae suspended in PBS, 1.0 μM BDP 1 with 15 min of irradiation completely abolished viability, whereas BDP 2 required only 2 min for the same outcome. In biofilms, BDP 1 produced ~ 1.5 log viability reductions after 60 min of white light. In contrast, BDP 2 caused ~ 2 log and ~ 3 log reductions in 18 h old biofilms at 5.0 and 10.0 μM , respectively, and completely eradicated cells when 10.0 μM was applied during proliferation followed by 60 min irradiation. These findings highlight the superior performance of BDP 2 across all *C. albicans* morphologies, underscoring its potential as an effective photosensitizer for antifungal PDI strategies.



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sciforum-152281: Promising Antitumor Agents: Synthesis and Cytotoxicity of New O-Dodecyl-Substituted Arylmethylidene Thiazolo[3,2-a]pyrimidines.

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Heterocyclic compounds containing the thiazolo[3,2-*a*]pyrimidine scaffold are of significant interest in medicinal chemistry due to their broad spectrum of biological activities. In recent years, this heterocyclic fragment has been shown to serve as a key structural unit for the development of new pharmacophores exhibiting antimicrobial, antibacterial, and anti-inflammatory properties. One effective strategy for modifying such molecules to improve their drug-like properties is the introduction of lipophilic fragments. The addition of a long-chain alkyl substituent, such as an *n*-dodecyl group, can significantly increase the compound's lipophilicity. This, in turn, facilitates better penetration through cellular membranes and enhances bioavailability, potentially amplifying the therapeutic effect.

Within the framework of this study, a four-step synthesis of novel O-dodecyloxybenzylidene derivatives of thiazolo[3,2-*a*]pyrimidine was designed and accomplished. The synthesis of the target compounds involved the following sequential stages:

- 1) Conducting a three-component Biginelli reaction to obtain the initial pyrimidinethione precursor.
- 2) Condensation of the resulting product with ethyl chloroacetate to form the thiazolo[3,2-*a*]pyrimidine core.
- 3) Knoevenagel condensation with *para*-hydroxybenzaldehyde, which introduced the benzylidene fragment and yielded the *para*-hydroxybenzylidene derivatives.
- 4) A key alkylation step via a Mitsunobu reaction with *n*-dodecyl alcohol, which allowed for the introduction of the lipophilic "tail" and afforded the target O-dodecyl derivatives.

The structure and high purity of all synthesized intermediate and final compounds were unambiguously confirmed by a comprehensive set of physicochemical analysis methods, including NMR spectroscopy (¹H and ¹³C), mass spectrometry, and IR spectroscopy.

The synthesized compounds were subjected to *in vitro* screening for antitumor activity against a panel of cancer cell lines, including M-HeLa, Hutu-80 and PC-3. It was demonstrated that the introduction of the *n*-dodecyl fragment indeed led to the emergence of biological activity. The obtained compounds exhibited moderate, yet statistically significant, cytotoxic activity against all tested cell lines.



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sciforum-142565: QSAR Analysis of 5,6-Dimethoxyindanone-Piperazine Derivatives as Potent Acetylcholinesterase Inhibitors

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Background: The cholinergic deficit in Alzheimer's disease (AD) is treated symptomatically with acetylcholinesterase (AChE) inhibitors, yet current drugs suffer from limited brain penetration and adverse effects. 5,6-Dimethoxyindanone constitutes the pharmacophore of donepezil; conjugation with piperazine yields analogues with promising activity. **Methods:** IC₅₀ values for fifteen dimethoxyindanone–piperazine derivatives were extracted from a study employing the Ellman assay and converted to pIC₅₀ for modelling. Three-dimensional geometries were energy-minimised (MM⁺ → PM3), and 4 885 Dragon descriptors calculated. After statistical filtering (low variance, excessive missing data, inter-correlation $r \geq 0.95$), 843 descriptors remained. Stepwise selection isolated four key variables—Mor22v, HATS8p, VE1_B(p) and C-006—encoding molecular volume, spatial polarizability, electronic distribution and CH₂RX fragments. An artificial neural network (MLP 4-3-1, BFGS) was trained on nine compounds, validated on three and externally tested on a further three. **Results:** The model reproduced experimental activity with $R^2 = 0.961$, $Q^2 = 0.999$ and MAE = 0.001 μ M; external prediction yielded $R^2_{\text{test}} = 0.928$. Sensitivity analysis ranked C-006 as the dominant contributor, indicating that strategic CH₂RX substitution at the indanone core drives potency, while Mor22v and VE1_B(p) emphasised the favourable impact of molecular volume and electron-withdrawing groups. **Conclusions:** This concise ANN-QSAR model delivers accurate, mechanism-based predictions and provides tangible design rules—enhanced polarizability, optimal volume and selective halogenation—for next-generation, brain-penetrant AChE inhibitors. The workflow is fully transferable to larger libraries and multi-target optimisation, paving the way for rapid, cost-effective exploration of indanone-based chemotypes in AD drug discovery.



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sciforum-142624: QSAR Analysis of Curcumin Analogues as Potent LSD1 Inhibitors with Anticancer Potential

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Background: Lysine-specific demethylase-1 (LSD1/KDM1A) erases mono- and dimethyl marks on histone H3 and is over-expressed in prostate, breast, and lung tumours, making it an increasingly attractive epigenetic target for anticancer therapy. Although the natural polyphenol curcumin inhibits LSD1 only weakly, its modular scaffold lends itself to systematic optimisation through computational chemistry. **Methods:** A previously published study compiled chemical structures and Ellman-assay IC₅₀ values for nineteen curcumin analogues. After three-dimensional geometry optimisation (MM⁺ → PM3), 4,885 Dragon descriptors were calculated; variance, missing-value, and multicollinearity filters ($r \geq 0.95$) reduced the pool to 763. Stepwise selection retained four informative descriptors—P_VSA_s_5, JGI8, H2s, and SpPosA_A—reflecting polar surface area, eighth-order topological charge, spatial polarizability, and positive fragment surface. A radial-basis-function artificial neural network (4-6-1 architecture) was trained on thirteen compounds, internally validated by leave-one-out cross-validation, and externally evaluated on a three-compound test set. **Results:** The model reproduced experimental potency with $R^2 = 0.999$, $Q^2 = 0.9996$, and MAE = 0.11 log units; external prediction yielded $R^2_{\text{test}} = 0.928$. Sensitivity analysis identified P_VSA_s_5 as the dominant contributor, indicating that enlarging the polar surface area in specific atomic states enhances enzyme binding, while the JGI8 descriptor underscored the importance of charge distribution. **Conclusions:** This compact, rigorously validated QSAR model offers accurate, mechanism-based predictions and actionable design rules—optimal polar surface area, favourable charge topology, and judicious halogenation—for next-generation LSD1 inhibitors, thereby accelerating epigenetic drug discovery pipelines.



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sciforum-152222: A Multitarget QSAR Approach for Virtual Screening of Natural Product and Drug Databases to Identify Novel Antifungals for Deep Mycose

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Deep mycoses are a type of fungal infection considered a neglected tropical disease by the World Health Organization (WHO), affecting at least hundreds of thousands of people around the world. While there are treatments for fungal diseases, the rise of antifungal resistance urges the research of novel antifungal agents. This study aims to discover new molecules from natural products and repurpose clinically evaluated drugs that present potential antifungal activity against deep mycoses pathogens, through the construction and deployment of machine learning models based on multitarget quantitative structure-activity relationships (QSAR). Using experimental IC₅₀ data from the ChEMBL database, 40 machine learning algorithms were tested, and the 5 best performing algorithms (Bagging, Gradient Boosting, LightGBM, Random Forest, XGBoost) were used to predict the antifungal activity of nearly 460,000 compounds from natural products as well as repurposing databases. This analysis resulted in the selection of 57 compounds considered active by consensus of the 5 models, including beta-lactams, griseofulvin derivatives and peptides, as well as standard antifungal drugs, such as amphotericin B and Nystatin, demonstrating the capability of the models to identify antifungal activity. Furthermore, the calculation of SHAP values provided mechanistic insight, confirming that the models' predictions were driven by molecular substructures characteristic of established antifungal agents. This study highlights potential antifungal agent candidates, both novel and repurposed, warranting further *in silico*, *in vitro*, and *in vivo* studies.



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sciforum-151669: A small molecule inhibitor of the main coronavirus protease 3CLPro based on a carbocyclically substituted peptidomimetic.

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The mechanism of action of peptide inhibitors involves two steps. 3CLpro inhibitors, which mimic natural peptide substrates, initially bind to 3CLpro and form a non-covalent complex, while the attacking group (warhead) undergoes a nucleophilic attack, forming covalent bonds with the Cys145 residue. In this paper, we present a new small-molecule inhibitor of the main coronavirus protease, 3CLPro, based on the carbocyclically substituted peptidomimetic N-(4-methyl-1-oxo-1-((1-oxo-3-(2-oxopyrrolidin-3-yl)propan-2-yl)amino)pentan-2-yl)-(2Z)-3-(thiophen-2-yl)prop-2-enamide (TEA-Leu-PId-CHO).

This low-toxicity compound (CC50 was 187.5 µg/ml) exhibits antiviral activity against modern coronavirus strains, including SARS-CoV-2. This substance exhibits sufficient solubility in aqueous solutions due to the one-step conversion of the aldehyde group to sodium bisulfite as a prodrug. To study the antiviral properties of the TEA-Leu-PId-CHO compound, the SARS-CoV-2 human coronavirus strain, passage 4, with an infectious activity of 106 TCID50/mL for Vero-E6 cells, was used.

An experiment to assess cell viability in the antiviral efficacy assay was conducted over a range of drug concentrations from 375.0 to 0.37 µg/mL, by titrating the initial concentration in the wells of a 96-well plate. The antiviral activity of the compounds was assessed visually under a microscope 96 hours after infection by inhibiting the viral CPE in a Vero E6 cell culture. The IC50 for TEA-Leu-PId-CHO was 5.8 µg/mL. Thus, Si was 32.

The proposed compound, given its high antiviral activity and low cytotoxicity, as well as its economic and synthetic availability, can be recommended as a candidate for preclinical and clinical trials to develop an etiotropic antiviral drug aimed at inhibiting an important enzyme—the main protease of the coronavirus, including modern strains of SARS-CoV-2.



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sciforum-151588: Activity, pharmacokinetics, and tissue distribution of 5-amino-N-tert-butyl-2-(methylsulfanyl)-4-(3-(nicotinamido)phenyl)thieno[2,3-d]pyrimidine-6-carboxamide (TP03), an allosteric agonist of the luteinizing hormone receptor

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Gonadotropin preparations with luteinizing hormone (LH) activity are widely used to stimulate ovulation, but they have a number of side effects. Low-molecular allosteric LH receptor agonists, including our developed compound TP03, may be an alternative. TP03 was obtained with the acylation of 5-amino-4-(3-aminophenyl)-*N*-(*tert*-butyl)-2-(methylthio)thieno[2,3-*d*]pyrimidine-6-carboxamide, and, according to high-resolution mass spectrometry, this MW was 515.1304 (the calculated MW for [M+Na⁺] was 515.1294). Being a hydrophobic compound, TP03 is able to penetrate the transmembrane tunnel of the LH receptor, interacting with the transmembrane allosteric site. The aim of this study was to investigate the effect of TP03 on ovarian steroidogenesis and ovulation in immature female rats, as well as to investigate its pharmacokinetics in blood plasma and its distribution in ovaries and liver. Immature female rats stimulated with Follimag were administered TP03 (15 mg/kg, i.p. in DMSO), after which the levels of estradiol and progesterone in blood and the number of preovulatory follicles and corpora lutea in ovaries were assessed for 24 h. Using reversed-phase HPLC with tandem mass spectrometry, TP03 levels were measured in blood plasma, ovaries and liver. TP03 increased blood progesterone levels and, after 16–24 hours, led to the formation of corpora lutea in ovaries. The maximum plasma concentration of TP03 was 3530 ng/mL, and the time to reach maximum concentration was 15 min, indicating rapid absorption of TP03. The elimination constant, characterizing the rate of TP03 elimination, was 0.24 h⁻¹, and the half-life of TP03 was 2.94 h. Thus, TP03 is a long-lived compound in the bloodstream. Rapid accumulation of TP03 in ovaries and liver was demonstrated 1 hour after administration. Thus, the high efficacy of TP03 as an ovulation inducer is largely due to its rapid absorption in ovaries and long half-life in the bloodstream. The study was supported by the RSF (No 19-75-20122).



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sciforum-151418: Antibacterial Potential of 2-Benzoylpyridine *N*-(bicyclo[2.2.1]hept-2-yl)thiosemicarbazone and Its Copper(II) Complexes Towards *Bacillus cereus*

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Bacillus cereus is a widespread Gram-positive bacterium that can cause severe foodborne illnesses, opportunistic infections, and even life-threatening conditions such as endophthalmitis and bacteremia. Its pathogenic potential, combined with the ability to produce toxins and form resistant spores, makes it a serious public health concern. In recent years, the problem has been exacerbated by the increasing occurrence of antibiotic resistance in *B. cereus*, which reduces the effectiveness of conventional treatments. Therefore, the discovery and development of new drug candidates with strong antibacterial activity against *B. cereus* is of great importance. Since thiosemicarbazones and their metal coordination complexes, especially copper(II) complexes are frequently associated with pronounced antibacterial properties, the objective of the present study was the synthesis of novel thiosemicarbazone-based complexes and the evaluation of their antibacterial efficacy against *Bacillus cereus*.

In the present study, we report the synthesis of 2-benzoylpyridine *N*-(bicyclo[2.2.1]hept-2-yl)thiosemicarbazone (HL) and three corresponding copper(II) complexes: [Cu(L)NO₃], [Cu(L)Cl], and [Cu(L)CHCl₂COO]. The design of the ligand was based on a camphor-derived structural fragment, chosen due to the ability of such derivatives to display enhanced biological activity compared to their parent natural products. The thiosemicarbazone was prepared through a two-step synthetic procedure, followed by complexation reactions with appropriate copper(II) salts in ethanol in 1:1 molar ratio.

To evaluate the antibacterial activity of the obtained compounds against *Bacillus cereus*, the broth microdilution method was used. The HL did not exhibit activity, however, its copper(II) complexes demonstrated strong results, surpassing the activity of Furacillinum, an antimicrobial drug used in medicine. The most active compound is complex [Cu(L)NO₃], with MIC and MBC values of 0.24 µg/mL, which is 20 times higher than the activity of Furacillinum.

This work was fulfilled with the financial support of the ANCD project 24.80012.5007.14TC.



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sciforum-152093: Atom-Based 3D-QSAR Modeling and Molecular Docking of Tadalafil Analogs as Potential Acetylcholinesterase Inhibitors for Alzheimer's Disease.

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Acetylcholinesterase (AChE) is a critical therapeutic target in the development of small-molecule inhibitors for Alzheimer's disease (AD), a progressive neurodegenerative disorder characterized by cognitive decline and cholinergic dysfunction. In this work, 37 tadalafil analogs were studied as potential Acetylcholinesterase (AChE) inhibitors using a combined atom-based three-dimensional quantitative structure–activity relationship (3D-QSAR) modeling and molecular docking approach. Molecular docking studies were performed using the Glide program to predict binding affinity within the AChE active site and to validate key interactions responsible for inhibitory activity. The constructed 3D-QSAR model demonstrated excellent statistical robustness and predictive accuracy, showing a high correlation for the training set ($R^2 = 0.975$, $SD = 0.190$, $F = 464.7$, $N = 29$) and strong predictive performance for the test set ($Q^2 = 0.809$, $Pearson(r) = 0.941$, $RMSE = 0.564$, $N = 8$) using three partial least squares (PLS) factors. Analysis of the 3D-QSAR contour maps revealed critical structural regions where steric and electronic features either enhance or hinder Acetylcholinesterase (AChE) inhibition, providing valuable guidance for rational drug design. Based on these insights, five new candidate molecules were proposed, among which compound X1 exhibited the highest predicted inhibitory activity. These results highlight the power of integrating 3D-QSAR modeling with docking analysis to identify, design, and optimize potent Acetylcholinesterase (AChE) inhibitors, providing a strong foundation for the discovery of novel anti-Alzheimer's agents.



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sciforum-152077: Bisdithiophosphonic acids and their salts with antibacterial and cytotoxic activities

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Bisdithiophosphonic acids and their derivatives are strong sulphur- and phosphorus-containing acids with complexing, membranotropic properties and anticipated bioactivity. These acids contain two dithiophosphoryl groups that can associate with basic compounds and metal ions to form organic salts with potential biocidal effects against pathological cells and organisms. In this work, resorcinol and 4,4'-propane-2,2-diyl-diphenol were used in the reactions with Lawesson's reagent to synthesize *O,O'*-(benzene-1,3-diyl)-1,3-bis(4-methoxyphenyl)dithiophosphonic and *O,O'*-[propane-2,2-diyl-bis(4,1-phenylene)-bis(4,4'-methoxyphenyl)dithiophosphonic) acids, respectively. The synthesized bisdithiophosphonic acids were converted into disodium and dipotassium salts as well as salts on the basis of (*S*)-(-)-nicotine, (8*R*,9*S*)-quinine, and (8*R*,9*S*)-quinidine. Structural characterization of the resulting compounds was carried out using ³¹P{¹H} and FTIR spectroscopies.

Antibacterial properties of these compounds were assessed in vitro using broth microdilution method. Disodium and dipotassium bisdithiophosphonates were found to be low active against *Staphylococcus aureus* with minimal inhibitory concentration (MIC) of 1250 µg mL⁻¹. *O,O'*-(benzene-1,3-diyl)-1,3-bis(4-methoxyphenyl)dithiophosphonic acid and its salt with (*S*)-(-)-nicotine showed increased antibacterial effect toward *Bacillus cereus* with MIC of ca. 78 µg mL⁻¹. Cytotoxicity of the compounds toward human prostate adenocarcinoma (PC-3) cells was additionally studied using resazurin assay upon 24- and 72-hour culture. The synthesized compounds decreased growth of the cancer cells with inhibitory concentrations in micromolar/submillimolar range. The results can be used for further structure evolution of bisdithiophosphonates with antibacterial and cytotoxic activities. This work was funded by the Academy of Sciences of the Republic of Tatarstan in 2024 according to the grant on conducting fundamental and applied research in scientific and educational organizations and enterprises of the real sector of the Republic of Tatarstan.



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sciforum-152186: Chiral dithiophosphonic acids with antibacterial properties

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The development of phosphorus-containing compounds with specific biocidal action and low toxicity profile is a promising direction in medicinal chemistry. Chiral properties of such compounds may contribute to their selective interactions with biological targets. In this study, racemic alcohols were reacted with 2,4-diaryl-1,3,2,4-dithiophosphetane-2,4-disulfides to yield chiral dithiophosphonic acids. O-2-Ethylhexyl-4-methoxyphenyldithiophosphonic acid **1** was prepared by the reaction of Lawesson's reagent with 2-ethylhexanol in benzene upon moderate heating. The reaction of diethyl malate with Lawesson's reagent was carried out at ambient temperature to form O-[1,2-di(ethoxycarbonyl)ethyl-1] 4-methoxyphenyldithiophosphonic acid **2**. The compound **1** was reacted with ammonia, (S)-(-)- α -methylbenzylamine, (R)-(+)- α -methylbenzylamine, α -methylbenzylamine, pyridine, and pyridoxine to give corresponding ammonium, chiral methylbenzylammonium, pyridinium, and pyridoxinium dithiophosphonates. Hexadecylammonium O-[1,2-di(ethoxycarbonyl)ethyl-1] 4-methoxyphenyldithiophosphonate was obtained by the reaction of the compound **2** with hexadecylamine.

The synthesized salts of dithiophosphonic acids were evaluated for their in vitro bacteriostatic/bactericidal properties against *Staphylococcus aureus*, *Bacillus subtilis*, and *Bacillus cereus* using broth microdilution method. According to minimal inhibitory concentrations (MIC) revealed, the compounds showed good antibacterial activity with MIC in the range from 7 to 116 $\mu\text{g mL}^{-1}$. Hexadecylammonium salt of dithiophosphonic acid on the basis of diethyl malate was the most effective against the bacterial growth. The study was supported by the Subsidy Allocated to Kazan Federal University for the State Assignment in the Sphere of Scientific Activities (project FZSM-2025-0002).



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sciforum-152315: CODRUG: An open-source graphical interface for Ligand-Based Drug Discovery using QSAR and Machine Learning

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Automated and user-friendly interfaces are essential in drug discovery, as they expand access to *in silico* tools for professionals without programming expertise and enable more laboratories to adopt virtual screening strategies. Advances in software and hardware have significantly improved the performance and accuracy of *in silico* methods applied to small molecule screening. Ligand-based drug discovery (LBDD), which explores structure–activity relationships (SAR) across large datasets, has increasingly incorporated machine learning (ML) and deep learning (DL) models, including artificial neural networks (ANNs). However, applying data science tools remains challenging for researchers in small laboratories, as it often requires programming expertise, integrated development environments (IDEs), or access to proprietary software. To address this gap, we developed CODRUG, an open-source, intuitive and flexible graphical user interface (GUI) designed to support ligand-based drug discovery. Together with CODOC (molecular docking interface) and CODYN (molecular dynamics interface), CODRUG forms a comprehensive softwares suite. The tool integrates into a screening pipeline that combines structure-based approaches (molecular docking and dynamics) with ligand-based methods (3D-QSAR), generating ranked compound lists for *in vitro* and *in vivo* validation. CODRUG was implemented in Python version 3.10.12 using PyQt5 and the Qt framework version 5.15.14. Its design uses sequential tabs covering the workflow: home, general settings, dataset preparation, preprocessing, exploratory analysis, descriptor generation, models screening, validation and hyperparameter tuning, prediction and result interpretation. This layout guides users through complex processes, reducing the need for coding expertise. By providing an accessible, open-source platform that incorporates advances in ML and DL, CODRUG lowers technical barriers and enhances efficiency of *in silico* screening. This contribution is expected to facilitate the identification of promising compounds and accelerate the development of novel therapeutic candidates. Next steps, CODRUG will be validated through case studies and integrated into collaborative pipelines, expanding its applicability in drug discovery.



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sciforum-152195: Design and Evaluation of Piperidine-Based Inhibitors targeting Alzheimer's Disease

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Introduction

Alzheimer's Disease (AD) is a neurodegenerative illness causing severe cognitive decline, personality changes, and psychological issues, with over 10 million new cases per year which are expected to double by 2036. The most widely prescribed drug to treat symptoms of AD is the cholinesterase inhibitor donepezil, first approved in the US in 1996. Donepezil's activity comes largely from its nitrogen-containing heterocyclic piperidine structure. The piperidine ring appears frequently in other compounds targeting AD and has prompted AD research into piperidine containing derivatives.

Method

In this work, computer-aided drug design (CADD) was used to virtually screen a library of 32 piperidine-containing molecules derived from a lead against co-crystallized human acetylcholinesterase (AChE) and human butyrylcholinesterase (BuChE). Based on docking scores and detailed 2D and 3D interactions with the target, the top eight derivatives were synthesized via N-alkylation reaction, and confirmed with ¹H-NMR and EI-MS. Their action on AChE and BuChE was determined via enzyme inhibition assay using Ellman's method.

Result

The IC₅₀ values of four derivatives showed significant action against both enzymes (MA13 [AChE IC₅₀=69.2 μM; BuChE IC₅₀=19.5 μM], MA29 [21.4; 13.2 μM], MA31 [20.4; 18.5 μM], MA32 [29.6; 23.5 μM]), while 2 within this group showed particularly strong inhibitory action against BuChE when compared with donepezil (MA29, MA31).

Conclusion

Overall, these results reveal new scaffolds with promising anti-Alzheimer's potential, including two candidates that show particularly strong activity against BuChE. Further development of these molecules may yield viable candidates for next-generation therapeutics, providing new opportunities to slow or lessen the progression of AD.



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sciforum-151738: Design and Synthesis of Bioactive Benzofused Nitrogen Containing Heterocyclic Derivatives

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Inflammation is a key pathological process underlying numerous acute and chronic disorders, and while non-steroidal anti-inflammatory drugs (NSAIDs) remain widely prescribed, their clinical utility is restricted due to adverse effects such as gastrointestinal bleeding, hepatotoxicity, and the emergence of resistance during prolonged therapy. To overcome these limitations, heterocyclic scaffolds have emerged as privileged structures in medicinal chemistry, with benzimidazole and oxadiazole derivatives showing strong potential as anti-inflammatory agents. In the present study, a series of benzofused nitrogen-containing heterocyclic derivatives were designed and synthesized by employing 2-mercaptobenzimidazole as the core pharmacophore. The synthetic pathway involved the initial formation of thioacetate from 2-mercaptobenzimidazole and ethyl-2-chloroacetate in ethanolic KOH, followed by hydrazinolysis to yield the corresponding acetohydrazide, which was subsequently cyclized with various substituted aromatic acids in the presence of H_2SO_4 to afford the final heterocyclic derivatives. Structural elucidation was achieved using FT-IR, 1H -NMR, and mass spectrometry, where spectral data confirmed the disappearance of primary amine/amide peaks and the appearance of diagnostic $C=N$, $C-O-C$, and secondary amine signals. Proton NMR spectra revealed characteristic $-CH_3/-CH_2$ resonances (1.0–4.0 ppm) and aromatic signals (7.0–9.0 ppm), while molecular ion peaks ($M+1$) in mass spectra validated the expected molecular weights. Toxicological evaluation using AOT 425 guidelines established an LD_{50} of 1103 mg/kg, suggesting an acceptable safety margin. Pharmacological screening via carrageenan-induced rat paw edema assay demonstrated that the synthesized compounds, administered at 110 and 130 mg/kg, produced significant inhibition of inflammation, comparable to standard reference drugs. Overall, the findings highlight the promising anti-inflammatory potential of the synthesized benzofused heterocycles and support further optimization for drug development.



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sciforum-152355: Design-Oriented Synthesis and Biological Evaluation of Melanostatin Neuropeptide Derivatives with Improved Pharmacokinetic Profiles

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Melanostatin (MIF-1) is a short endogenous neuropeptide that acts as a highly selective positive allosteric modulator (PAM) of human dopamine D₂ receptors (*hD₂R*), exhibiting significant clinical potential for the treatment of dopamine-related central nervous system (CNS) disorders, including depression, drug addiction, obesity, restless legs syndrome, tardive dyskinesia, and Parkinson's disease. Preliminary studies have shown that substitution of the L-proline residue with L-pipecolic acid generates bioactive derivatives, highlighting the importance of this residue for PAM activity.

In this work, we further explored the role of the L-proline residue by fusing the structural features of L-proline and L-pipecolic acid into a bridged chimera scaffold, (1*R*,3*S*,4*S*)-2-azanorbornane-3-carboxylic acid, and designed a series of 16 bridged melanostatin derivatives to enhance PAM activity and improve pharmacokinetic properties. A concise stereoselective synthetic route afforded the target compounds in high overall yields, with absolute stereochemistry confirmed by X-ray crystallography.

Functional assays at *hD₂R* identified four compounds exhibiting potent PAM activity at 0.01 nM, producing a 5- to 6.6-fold increase in dopamine potency. Toxicological profiling in HepG2 and differentiated SH-SY5Y neuronal cells revealed no hepatotoxicity (up to 100 µM) and generally favorable neurotoxicological profiles (up to 200 µM). Permeability studies demonstrated negligible P-glycoprotein interaction and favorable Caco-2 transport, suggesting improved CNS penetration relative to the parent neuropeptide.

Collectively, these findings establish 2-azanorbornane as a privileged scaffold for the development of potent, selective, and brain-penetrant PAMs targeting *hD₂R* signaling. This work provides a strong basis for the discovery of novel therapeutics for dopamine-related neurological disorders, combining enhanced pharmacokinetic properties, safety, and high PAM efficacy.



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sciforum-152353: Design, Synthesis, and Biological Evaluation of Sila-Derivatives of Vitamin D with Application in Breast Cancer Therapy

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The strategic incorporation of silicon into bioactive molecules has emerged as an effective approach to enhance drug properties, including metabolic stability and target specificity. However, no secosteroidal vitamin D receptor (VDR) ligands containing silicon have been reported to date. Here, we describe the rational design, synthesis, and biological evaluation of six novel analogues of 1,25-dihydroxyvitamin D₃ (1,25D₃), in which a silicon atom is introduced as an isosteric replacement at the C25 side chain position.

The sila-derivatives were synthesised via a Wittig-Horner approach starting from the Inhoffen-Lythgoe diol, enabling precise silicon incorporation at the C25 position of the side chain, while preserving the stereochemistry of the secosteroidal structure. X-ray crystallographic analysis of VDR ligand-binding domain complexes (PDB codes 9GY8, 9GYJ, 9GYC, 9GYA, and 9GYK, available at Protein Data Bank) revealed additional stabilising interactions mediated by the silicon-containing side chains, supporting the receptor's active conformation.

Functional assays showed that these analogues maintain VDR binding and transcriptional activity comparable to 1,25D₃, while exhibiting markedly lower hypercalcaemic effects in cellular models. Notably, in combination with conventional chemotherapeutics, the analogues significantly reduced cancer cell proliferation, indicating potential synergistic effects.

Overall, these results provide a framework for the development of silicon-modified secosteroidal VDR ligands with improved safety and therapeutic potential, highlighting new avenues for applications in both metabolic and cancer-related contexts.



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sciforum-151614: Development of amino-alcohol-quinolines targeting lung diseases caused by non-tuberculous mycobacteria.

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The emergence of non-tuberculous mycobacteria (NTM) infections is outstripping that of *Mycobacterium tuberculosis*. Some species cause opportunistic infections in humans. In people with bronchiectasis or chronic respiratory disease, 80% of infections are related to NTM, and among these, *Mycobacterium avium complex* (MAC) is the most common. Guidelines-based treatment consists of a combination of a macrolide, a rifamycin and ethambutol. This treatment is prescribed for at least 12 months and its effectiveness is estimated at 52%, due to the development of macrolide resistance in MAC. These drugs can cause inconveniences or serious effects. Drug interactions can also occur, e.g., clarithromycin and rifampicin are strong inducers of cytochrome P450. Consequently, there is an urgent need to develop safer molecules with novel mechanisms of action that also minimize the risk of antibiotic resistance.

The quinoline-based pharmacophore is found in mefloquine (MQ). MQ has moderate anti-NTM activity *in vitro* (MIC = 4 µg/mL on MAC), high *in vitro* toxicity (CC₅₀ = 2.6 µg/mL on HepG2 cells) and a low maximum tolerated *in vivo* dose (40 mg/kg).

Our aim is to develop new amino-alcohol-quinolines (AAQ), analogues of MQ, by modulating the structural positions of the MQ core, particularly the amino-alcohol chain, in order to improve efficacy and reduce toxicity. Two series of AAQ were developed and thirty-one compounds were obtained. One hit was identified, with the highest selectivity index (SI) on *M. avium* (SI = 5.8). Additionally, checkerboard assay was demonstrated an additive effect with the antibiotics used in the reference treatment. Finally, this hit was evaluated in BALB/c mice and excellent tolerance was revealed (tolerate dose ≥ 500 mg/kg).

The following topics will be presented: i) the design and synthesis of AAQ, ii) their *in vitro* activity and toxicity, iii) the potential *in vitro* synergistic effects of one *hit* compound, and iv) the *in vivo* toxicity of this promising compound.



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sciforum-149955: Development of Kojic Acid–3-Hydroxyindolin-2-one Conjugates: Structural Characterization and Pharmacological Evaluation

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Kojic acid (KA), a natural compound with notable biological properties, is a versatile scaffold (*5-hydroxy-2-(hydroxymethyl)-4H-pyran-4-one*) for developing novel therapeutic agents. This study aimed to synthesize KA-based derivatives and evaluate their multifunctionality as anti-tyrosinase, anticancer, antioxidant, and anti-malarial agents. Exploring KA derivatives holds promise for advancing in skin brightening, malaria, and cancer therapeutics, and managing oxidative stress, addressing the demanding need for multifunctional compounds in modern medicine. KA derivative (DRC-01) was synthesized through one-pot aldol condensation chemical reactions and structurally confirmed using advanced spectroscopic techniques, including FTIR, NMR, and mass spectrometry. The anti-tyrosinase activity on Mushroom Tyrosinase protein from RCSB PDB (PDB: 2Y9X) and anticancer potential were evaluated in vitro using the MTT assay against human cancer cell lines: HCT-116 (colon cancer), PANC-1 (pancreatic cancer), MDA-MB-231 (triple-negative breast cancer), and MCF-7 (hormone-responsive breast cancer). Antioxidant activity was assessed using the DPPH assay to determine radical scavenging properties, and the Antimalarial activity was performed by SYBR GREEN assay in *Plasmodium falciparum* 3D7. DRC-01 showed binding energy -7.4kcal/mol compared to standard KA -5.8kcal/mol and dose-dependent cytotoxicity, demonstrating anticancer activity at higher concentrations (>50 μ M) across all tested cell lines. Additionally, DRC-01 displayed moderate radical scavenging activity in the antioxidant assay, and Antimalarial potential was at $IC_{50} = 54.94 \pm 3.11 \mu$ g/mL. These findings highlight that DRC-01 could be a candidate for therapeutic applications with its cosmeceutical properties. Further structural optimization is acceptable to enhance their potency and selectivity, reinforcing their value in the fight against cancer, malaria, and oxidative stress-related disorders.



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sciforum-149335: Dopexamine as a Multitargeted Drug Candidate for *E. coli* caused Urinary Tract and Bloodstream Infections and Outperforms FDA-approved Drugs Nitrofurantoin and Ceftriaxone

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Abstract: The increasing problem of antimicrobial resistance (AMR) has made it more difficult to treat even common infections, especially Urinary Tract Infections (UTIs) and Bloodstream Infections (BSIs). These infections are often caused by bacteria resistant to multiple antibiotics, limiting treatment options. Among the most common pathogens responsible for these infections is *Escherichia coli* (*E. coli*), which has shown increasing resistance to several frontline antibiotics. In this study, multitargeted docking of the FDA-approved library from DrugBank was performed against crucial proteins from *E. coli* such as FimH (PDB ID: 1UWF), PNAG N-deacetylase (PDB ID: 4F9D), and Purine nucleoside phosphorylase (PDB ID: 4TS3) involved in UTIs, and BtuF (PDB ID: 1N4A), Uridine phosphorylase (PDB ID: 1RXC), and LpxH (PDB ID: 8QJZ) involved in BSIs. This study explored the potential of repurposing Dopexamine, a drug initially used to support heart function, as a possible solution to target key bacterial proteins involved in AMR. An in-silico approach was employed to investigate Dopexamine's ability to inhibit mutated bacterial proteins associated with *E. coli*-mediated UTIs and BSIs. Comprehensive computational analyses were performed, including molecular docking to assess binding interactions, molecular dynamics (MD) simulations to evaluate complex stability, MM/GBSA (Molecular Mechanics/Generalized Born Surface Area) calculations to evaluate binding free energies, Water Map analysis to understand hydration patterns, and Density Functional Theory (DFT) to investigate the electronic properties of Dopexamine. The results revealed favourable binding affinities, stable interactions, and promising physicochemical properties, indicating Dopexamine's potential as a broad-spectrum inhibitor against AMR-related targets. These findings suggest Dopexamine as a valuable candidate for drug repurposing.



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sciforum-152040: Dual Inhibition of AChE and Amyloid- β Aggregation by 3-Vinyl-Quinoxalin-2(1H)-one Derivatives for Alzheimer's Therapy

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A series of derivatives based on 3-vinyl-quinoxalin-2(1H)-one were designed, synthesized, and screened for their dual activity against amyloid beta (A β) aggregation and human acetylcholinesterase (hAChE). In this comprehensive study, sixteen compounds were meticulously evaluated using the Ellman assay, revealing that MHA-2 and MHA-15 emerged as the most effective inhibitors of hAChE, exhibiting low micromolar IC₅₀ values. These values highlight the compounds' ability to inhibit the enzyme at remarkably low concentrations, suggesting high potency. To further investigate, the molecular docking and dynamics simulations were conducted. These computational approaches provided additional support for the experimental findings, revealing stable interactions with key catalytic and peripheral residues of hAChE enzyme. Furthermore, PAMPA-BBB (Parallel Artificial Membrane Permeability Assay for the Blood-Brain Barrier) analysis confirmed their favourable blood-brain barrier permeability, while competitive displacement of propidium iodide indicated strong binding at the peripheral anionic site (PAS) of hAChE. Moreover, the Thioflavin T fluorescence assays demonstrated that both compounds effectively suppressed A β aggregation, inhibiting not only spontaneous self-assembly but also hAChE-induced fibrillization in a concentration-dependent manner. In conclusion, the compounds MHA-2 and MHA-15 emerge as promising lead scaffolds with dual functionality in hAChE inhibition and A β aggregation prevention, coupled with favourable BBB permeability, supporting their potential as therapeutic candidates for Alzheimer's disease.



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sciforum-152138: Dual Inhibition of COX-2 and 5-LOX by Novel 4-Aminoacetanilide Derivatives: Insights from Synthesis, Bioassays, and Molecular Docking

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Introduction

Inflammatory disorders remain a major therapeutic challenge, with current treatments (NSAIDs, corticosteroids) often limited by safety concerns. The inflammatory cascade is largely driven by cyclooxygenase (COX) and lipoxygenase (LOX) pathways. Dual inhibition of COX-2 and 5-LOX has emerged as a promising strategy to achieve effective anti-inflammatory activity with reduced side effects. Acetamide derivatives are known to exhibit diverse medicinal effects.

The present study is based on the synthesis and evaluation of 4-aminoacetanilide scaffolds towards COX-2 and 5-LOX inhibition.

Method

The inhibitory activity of eight synthesized 4-aminoacetanilide derivatives was assessed against COX-2 and LOX using fluorometric and spectrophotometric assays, respectively. IC₅₀ values were determined and compared with the reference drugs Aspirin (COX-2) and Baicalein (LOX). Additionally, molecular docking studies were performed to elucidate the binding interactions of the most active compounds within the catalytic sites of COX-2 and LOX.

Results

AI-06 showed notable potency against COX-2 (IC₅₀: 31.2 μM), while AI-02, AI-03, and AI-06 demonstrated strong inhibition of LOX with IC₅₀ values of 14.1, 19.2, and 26.5 μM, respectively. Structure–activity relationship (SAR) analysis indicated that both the position and nature of substituents played a critical role in determining inhibitory activity. Molecular docking further revealed key binding interactions responsible for the observed potency.

Conclusion

The findings suggest that AI-02, AI-03, AI-06, and AI-08 hold promise as dual COX-2/5-LOX inhibitors and could be further optimized as potential anti-inflammatory agents.



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sciforum-152037: Enantiopure 4-aminoalcohol-pyridines as potent antimalarial agents: synthesis and biological evaluation

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Malaria remains a major global public health challenge, particularly in sub-Saharan Africa. According to the World Health Organization, an estimated 263 million cases of malaria and approximately 597,000 deaths were reported in 2023. The disease is caused by *Plasmodium* parasites, transmitted through the bites of female *Anopheles* mosquitoes. Among the five species infecting humans, *P. falciparum* remains both the most prevalent in Africa and the most lethal. Over the past century, *P. falciparum* has progressively developed resistance to artemisinin-based combination therapies (ACT), the current front-line treatment recommended by the WHO.

This resistance correlates with mutations in the *pfk13* gene, associated with artemisinin resistance, as well as alterations in *Pf* multidrug resistance 1 (*PfMDR1*), a transporter which regulates the influx of nutrients and molecules, including arylaminoalcohols, into the parasite's digestive vacuole. These changes weaken the efficacy of ACT, ultimately reducing the overall effectiveness of the treatment and highlighting the urgent need to discover new effective antimalarial agents.

Herein, we report the design and synthesis of enantiopure aminopyridine derivatives built on the enpiroline scaffold as promising antimalarial compounds. Their optimized synthesis route and key physicochemical properties will be outlined, followed by an evaluation of their *in vitro* biological activity. Most of the compounds display potent *in vitro* inhibition close to the nanomolar range against both 3D7 and W2 *P. falciparum* strains. Cytotoxicity assays showed excellent selectivity indices, mostly above 500. A structure-activity relationship analysis will also be presented, offering valuable insights for further optimization.



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sciforum-152298: Exploring Drug Repurposing for COVID-19: Investigating acridinium's potential Effects on $\alpha 7$ nAChR

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COVID-19 has caused over 7 million deaths worldwide. The virus binds to ACE2 receptors, and disease progression can trigger a cytokine storm, an intense inflammatory response linked to a higher mortality rate. Given the potential role of $\alpha 7$ nAChR in modulating anti-inflammatory pathways, this study investigates its agonists and their interactions, integrating pharmacophore modeling for virtual screening of FDA-approved drugs. Initially, EVP-6124 was redocked into 7EKP to establish a docking protocol. Subsequently, the 7EKI model underwent a 100 ns MD simulation, followed by cluster analysis to identify the most representative conformation for docking EVP-6124. The best docking pose was then subjected to a 500 ns MD simulation until convergence. Pharmacophore models derived from representative conformations were validated using ROC curves, yielding scores above 0.8. These models guided the screening of FDA-approved compounds, with top candidates further evaluated via MD simulations. To do so, all results were docked using GOLD and evaluated with GoldScore, ChemScore, ChemPLP, and ASP scoring functions. For each function, 100 poses were generated and clustered within 2 Å. Representative clusters were rescored using GNINA, and the top-scoring pose was selected for MD simulation. While additional compounds remain under evaluation, this approach highlighted acridinium as a potential ligand for $\alpha 7$ nAChR, sustaining receptor interactions for up to 300 ns so far.



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sciforum-151628: From the design to the biological evaluation of quinoline-based carboxamides targeting non-tuberculous mycobacteria

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In recent years, non-tuberculous mycobacterial infections are definitely increasing worldwide. In particular, in Europe and North America, the non-tuberculous mycobacteria's (NTM) incidence exceeds that of tuberculosis, with 1.0 to 1.8 case per 100,000 individuals. NTM are commonly found in the environment (soils, natural or urban water sources) and can be defined as opportunistic bacteria. Known for their pulmonary pathogenicity, several NTM can be particularly harmful to people with weakened immune system or pre-existing lung diseases such as cystic fibrosis, bronchiectasis or chronic obstructive pulmonary disease (COPD). The NTM classification is based on their type of growth: the slow-growing species include *Mycobacterium avium* complex (MAC), *M. xenopi* and *M. kansasii*, while *M. abscessus* and its MABSC complex and *M. fortuitum* belong to the rapid-growing species. Treatment options require a combination of three antibiotics including a macrolide, which depend on the strain. The treatment covers 18 to 24 months, with many associated side effects, and the cure rate remains moderate (e. g. 52 % to 60 % for MAC infections). Otherwise, mycobacterial resistance to macrolides, in particular MAC, represents a major challenge in treating infections. Our drug discovery strategy focuses on the development of a novel family of antibiotics based on a quinoline core, targeting NTM. Some developed or commercial antibiotics such as bedaquiline (BQ) or mefloquine (MQ) containing this scaffold have shown potent antimycobacterial activity. Thus, this work aims to design and synthesize innovative quinoline-based carboxamides, bearing an amide function on the position 4 of the quinoline ring. In addition, the determination of physico-chemical properties and the biological evaluation of synthesized compounds will be presented.



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sciforum-151528: Hydroxybenzoic acid esters as dual antioxidant and anti-neuroinflammatory agents: *in silico* and *in vitro* evaluation

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Neuroinflammation, primarily mediated by activated microglia, plays a central role in the onset and progression of neurodegenerative diseases. In search of effective modulators of these processes, we investigated the antioxidant and anti-neuroinflammatory potential of hydroxybenzoic acid esters. A library of 42 esters and their three parent acids was evaluated through molecular docking against proteins of the lipopolysaccharide (LPS) signaling pathway, including LPS-binding protein (LBP), CD14, and TLR4/MD2. The best-scoring compounds were synthesized and subjected to *in vitro* validation. Several derivatives, particularly isopentyl, octyl, and benzyl esters of 2-, 2,4-, and 3,4,5-hydroxybenzoic acids, demonstrated favorable docking interactions and were further examined. Antioxidant assays (ABTS and DPPH) revealed radical scavenging activities comparable to vitamin C, with 3,4,5-hydroxybenzoic derivatives exhibiting the highest efficacy. In BV2 microglial cells, selected esters reduced reactive oxygen species (ROS) and nitric oxide (NO) production following stimulation with hydrogen peroxide or LPS, thereby restoring cellular metabolic activity. Furthermore, supernatants from ester-treated microglia attenuated neurotoxicity in SH-SY5Y cells, confirming their neuroprotective effects. Importantly, these compounds displayed no cytotoxicity toward fibroblasts or microglia at tested concentrations, supporting their biocompatibility. Taken together, this study highlights hydroxybenzoic acid esters as promising multifunctional agents with dual antioxidant and anti-neuroinflammatory properties. Their ability to modulate microglial activation and protect SH-SY5Y cells suggests potential therapeutic relevance in managing neurodegeneration. Future work will focus on *in vivo* validation and preclinical development to advance these compounds toward medicinal applications.



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sciforum-152080: Identification of Novel Benzimidazole-Based NS5B Polymerase Inhibitors of Hepatitis C Virus Using Molecular Docking, Atom-Based 3D-QSAR Model, and ADMET Prediction

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Hepatitis C virus (HCV) remains a major global health threat, and the non-structural 5B (NS5B) polymerase is a key target for antiviral drug discovery. In this study, a virtual screening strategy was applied to identify novel benzimidazole-based inhibitors of the NS5B polymerase. Molecular docking was first performed to evaluate the binding affinities of a series of benzimidazole derivatives toward the NS5B polymerase active site. Key interactions of the ligand with the receptor active site were identified, displaying common features with those reported for other known inhibitors, thereby reinforcing the validity of the findings. An atom-based three-dimensional quantitative structure–activity relationship (3D-QSAR) model was subsequently developed and found to be statistically robust, with high predictive performance for both the training set ($R^2 = 0.95$, $SD = 0.18$, $N = 42$) and the test set ($Q^2 = 0.79$, $RMSE = 0.57$, $N = 11$). Guided by these findings, new benzimidazole derivatives were designed as potential NS5B polymerase inhibitors. The most promising compounds were further evaluated for their absorption, distribution, metabolism, excretion, and toxicity (ADMET) properties using pkCSM. to assess drug-likeness. This integrated computational approach provides valuable insights into the molecular features governing benzimidazole NS5B binding and identifies promising lead compounds for the development of new hepatitis C virus (HCV) therapeutics.



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sciforum-146468: Impact of Ferrocene and Ferrocenium on Cell Death Pathways in MCF-7 Cells

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Ferrocene is an organometallic compound that consists of an iron(II) ion linked to two cyclopentadienyl rings in a sandwich structure. This unique arrangement gives ferrocene remarkable stability and properties that make it valuable for various applications, including bioorganometallic chemistry. Several ferrocenyl-containing pharmacophores have been studied, such as ferrocifens, analogues of the anticancer tamoxifen, and ferroquine, an analogue of antimalarial chloroquine. Besides the specific activity of the organic portion of the ferrocene derivatives, such molecules are able to generate reactive oxygen species (ROS): $\text{Fe(II)/Fe(III)} + \text{H}_2\text{O}_2 \rightarrow \text{Fe(III)/Fe(II)} + \text{HO}^\bullet/\text{HOO}^\bullet + \text{H}_2\text{O}$.

ROS play a paradoxical role in disease progression: while elevated ROS levels are implicated in the onset of various pathologies, they act as tumor-suppressive agents involved in the mechanism of action of many chemotherapeutics. ROS generation is involved in many forms of programmed cell death, a group of self-protective cellular mechanisms triggered by external stimuli. Therefore, a fragile equilibrium is operating in healthy cells, where ROS can either promote or inhibit tumor development.

The activation of cell death pathways (i.e., apoptosis, necroptosis and ferroptosis) by ferrocene (Fc) and its monocation ferrocenium (Fc⁺) has been investigated in triple-negative breast cancer MCF-7 cells using immunofluorescence, flow cytometry, and transmission electron microscopy.

The distinct capabilities of Fc and Fc⁺ to generate ROS and trigger oxidative stress were evident through the activation of apoptosis, along with morphological changes following treatment of MCF-7 cells, particularly with Fc⁺. Fc⁺ induced ferroptosis within 2 h exposure, whereas Fc did not. Conversely, the more stable Fc initiated necroptosis after prolonged treatment.

Differences in cell death mechanisms and timing of Fc and Fc⁺ may arise from the rapid interconversion between Fe(II) and Fe(III). Fc and Fc⁺ can be promising candidates to address the limitations of conventional apoptosis-based cancer therapies.



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sciforum-151026: In Silico Assessment of Diketopiperazines as Potential Therapeutic Scaffolds for NTSR1

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Diketopiperazines (DKPs) are small, conformationally constrained cyclic dipeptides that have emerged as versatile scaffolds in drug discovery. Their rigid structures, chemical stability, and ability to mimic peptide backbones allow them to engage protein targets with high specificity, making them attractive candidates for receptor modulation. In particular, DKPs can overcome limitations of linear peptides, such as enzymatic instability and conformational flexibility, thereby offering improved pharmacological potential [1].

In this study, we investigated five Type 3 DKPs as potential modulators of Neurotensin Receptor 1 (NTSR1), a Class A G-protein coupled receptor (GPCR) implicated in neurological processes, pain regulation, and cancer progression [2]. The crystal structure of NTSR1 (PDB ID: 4GRV) was used as the receptor model, and molecular docking was performed with AutoDock 4.2 to assess peptide–receptor interactions [3]. All five DKPs demonstrated favorable binding energies, ranging from -4.31 to -7.83 kcal/mol, and engaged key residues within the orthosteric binding pocket. Notably, the compound HIJBAD exhibited the strongest predicted affinity (-7.83 kcal/mol), supported by a network of hydrogen bonding and hydrophobic interactions that suggest enhanced receptor stabilization.

These findings provide evidence that DKPs can serve as stable peptide-mimetic ligands capable of targeting GPCRs such as NTSR1. This work highlights their potential as chemical probes or lead scaffolds for the development of therapeutic agents in neurodegeneration and cancer. Further computational and experimental validation will be essential to fully establish their pharmacological relevance.

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sciforum-152107: In silico evaluation of natural nothoapiol derivatives for antioxidant activity

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Medicinal plants have long been recognized as valuable sources of natural compounds with significant therapeutic potential. They contain a wide variety of bioactive secondary metabolites, such as alkaloids and phenolic compounds, many of which serve as lead molecules in modern drug discovery. Owing to their structural diversity and broad spectrum of biological activities, these natural products represent an essential resource for developing novel drugs with enhanced efficacy and reduced side effects. In particular, numerous plant-derived compounds have demonstrated promising inhibitory effects against key enzymes, including xanthine oxidase (XO). XO is a crucial enzyme in purine metabolism, catalyzing the oxidation of hypoxanthine to xanthine and subsequently to uric acid.

In this study, three nothoapiol derivatives derived from essential oils were extracted from the medicinal plant *Petroselinum sativum* by V. Samet et al. These compounds exhibited excellent *in vitro* antioxidant activity. To further elucidate their mechanism of inhibition and evaluate their potential as XO inhibitors, an *in silico* molecular docking study was performed. Docking simulations were carried out using Schrödinger Suites 2023, with Glide employing the extra-precision (XP) docking protocol.

The docking results revealed that the nothoapiol derivatives exhibited strong binding affinities, with docking scores comparable to that of quercetin, a well-known standard XO inhibitor. Detailed interaction analysis demonstrated the formation of hydrogen bonds, hydrophobic interactions, and π - π stacking with key active site residues such as Ser876, Lys771, Phe1013, and Glu802, which are critical for XO catalytic activity. These findings suggest that the structural features of the nothoapiol derivatives particularly the presence of hydroxyl and methoxy substituents play a crucial role in enhancing binding stability and specificity.



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sciforum-151597: In Silico Evaluation of Novel Oxaprozin-Based Anti-Inflammatory Agents Targeting Cyclooxygenases

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Conventional medical therapy of inflammatory diseases relies on the use of non-steroidal anti-inflammatory drugs that reduce fever, pain, and other symptoms of inflammation. The mechanism of action of these drugs involves inhibition of cyclooxygenase (COX) enzymes, which mediate prostaglandin synthesis. However, severe adverse effects, particularly on the gastrointestinal tract, highlight the need for safer gastroprotective agents that selectively suppress inflammatory cytokine production. The aim of the study was to evaluate the binding affinities of five novel oxaprozin derivatives and the reference drug against the COX-1 and COX-2 isoenzymes. Ligand conformer data were generated using *OMEGA*, while molecular docking was performed using the *OEDocking* software, employing the *FRED* algorithm for fast exhaustive rigid docking. Docking results revealed that in the COX-1 active site, compounds **2** and **4** showed the lowest docking scores, comparable to oxaprozin (positive control), while compound **5** exhibited considerably higher values. Compounds **1** and **2** demonstrate similar behavior in the COX-2 binding pocket, forming a conventional hydrogen interaction with Ser353, π -cation electrostatic interaction with Arg120, several hydrophobic interactions with Val349, Leu352, Leu359, Val523, and Ala527. In addition, compound **2** establishes conventional hydrogen bonds with His90 and Arg513, further stabilizing the enzyme-ligand complex and likely accounts for its more favorable docking score compared to oxaprozin.



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sciforum-151340: In silico identification of a new potential drug-binding pocket on the surface of the receptor-binding domain of the SARS-CoV-2 S-glycoprotein

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SARS-CoV-2 is an emerging pathogen that caused the largest pandemic in modern history in 2020-2023. The surface S-glycoprotein, namely its RBD, significantly determines the pathogenesis of this virus: it allows SARS-CoV-2 to target human cells and ensures its internalization. Thus, the search for RBD inhibitors is currently considered a promising strategy for the drug development against COVID-19. In this work, we identified a new pocket on the RBD surface that could potentially bind small drug-like ligands. The FDA-approved drug compound library obtained from e-Drug3D was used as a source of drug-like chemical structures. The compounds were initially filtered by molecular weight (100-500 Da) using the Open Babel GUI. This allowed to reduce the size of the library from 2,118 to 1,749 compounds. Next, all filtered structures were docked to the RBD (PDB ID: 7T9L) using AutoDock Vina 1.1.2. The docking area was the entire RBD. **Results and conclusions:** We obtained a map of the uneven placement of ligands with different affinities to the target. The pocket formed by amino acids R454, R457, K458, S459, D467, S469, E471, I472, Y473, Q474, P479, N481, G482 and P491 was identified close to the functionally important ACE2-binding site of the RBD. It was able to interact with 128 ligands with the best estimated affinity of -7.8 kcal/mol for Oxymetholone. The latter interacted with the pocket through its hydroxyl and keto groups.

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sciforum-150777: Integrated Computational Assessment of Novel NDM-1 Inhibitors through Molecular Docking, Molecular Dynamics, and MM/GBSA Analysis

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The growing spread of NDM-1-producing bacteria represents a critical threat to the clinical efficacy of β -lactam antibiotics, including carbapenems, which are considered last-resort drugs. The continuous emergence of resistant strains underscores the urgent need to identify novel inhibitors capable of restoring the effectiveness of these antibiotics. In this study, a comprehensive computational protocol was applied to evaluate the inhibitory potential of four candidate compounds (M1, M2, P3, and P4) against the metallo- β -lactamase NDM-1. The workflow included 100 ns molecular dynamics simulations to explore the conformational stability of each complex, complemented by structural stability analyses (RMSD, RMSF), residue–ligand distance monitoring, and assessment of hydrogen bond evolution. Binding free energy calculations using the MM/GBSA approach were further conducted to provide thermodynamic insights into ligand affinity and complex stability.

The results demonstrated that compounds M2 and P4 exhibited superior dynamic behavior, maintaining stronger and more persistent interactions with catalytically relevant residues of the enzyme. These findings were reinforced by more favorable mean ΔG_{bind} values (–13.56 and –16.72 kcal/mol, respectively), suggesting robust binding affinity. Additionally, structural superimpositions over simulation time revealed distinct adaptive capacities of the ligands to the catalytic pocket, highlighting potential differences in their inhibitory mechanisms. Overall, the study positions M2 and P4 as promising scaffolds for the rational development of next-generation NDM-1 inhibitors. Moreover, the findings validate the utility of multivariate *in silico* approaches that integrate molecular dynamics, free energy calculations, and interaction mapping as powerful tools to prioritize candidates for experimental testing, ultimately supporting innovative strategies to counteract bacterial resistance.



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sciforum-152251: Ionic liquids modifications with oligosaccharides as potential drugs anticancer; molecular docking and DFT modeling enhancing the result

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The ionic liquid methyl imidazolium ethyl amine (MIE-NH₂) and its derivatives display a new role of modification of glycoproteins and oligosaccharides through a reductive amination mechanism for synthesizing versatile pharmaceuticals. This work focuses on the green processing of synthesis of the small molecules-ionic liquid (O-GLc-SMol-ILs), to be good applicable materials with significant bioactive properties as potential drugs anticancer. The MIE-NH₂ ionic liquids derivatives as intermediates for derivatization reaction with oligosaccharides in aqueous solution, which the new provide of oligosaccharides-ionic liquid enhancing its identification. The characterization and identification of small molecules ionic liquids linked to oligo- saccharides by LCMS, GCMS, NMR, UV-vis spectrophotometer. Bio-assay *in vitro* is the major aim promoted of this research. The evaluation of biologically active products is a significant challenge of these achievements and investigation. Using chemometric-modelling DFT-calculation for enhancing the interaction and SAR results. Particularly, the modified products (O-GLc-SMol-ILs) a small molecules is synthesized as anticancer activity, protein kinase B selected as a good target for interaction. New binding to protein kinase B was investigated through molecular docking to dig out their probable anticancer activity. All the products found with an exhibited the highest binding and potential inhibiting. This work will extend to study the potential effectiveness of (O-GLc-SMol-ILs) with liver cancer involving specific HepG2 cell lines via antiproliferative activity and autophagy candidate genes.



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sciforum-152244: Machine learning based approach to develop potential dual inhibitors of Neprilysin and Dipeptidyl peptidase-4: Implication in the treatment of type 2 diabetes

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Neutral endopeptidase (NEP or neprilysin) is a key enzyme associated with the metabolic inactivation of numerous bioactive natriuretic peptides (NP). Among these, bradykinin, endothelin, angiotensin II, amyloid β protein, substance P and glucagon-like peptide 1 (GLP-1) are the key NPs that affect the heart, kidney, and other organs. Among these, GLP-1, an essential simulator of insulin secretion, is frequently found to be impaired or downregulated in the case of diabetes, particularly type 2 diabetes. The level of GLP-1 is also diminished by another serine protease, Dipeptidyl peptidase-4 (DPP-4). Utilizing this concept of NEP and DPP-4 in orchestrating the degradation of the GLP-1 level and consequently affecting the type 2 diabetes outcome, we developed dual NEP/DPP-4 inhibitors that could offer an alternative regimen for treating type 2 diabetes.

In the present study, we have developed a machine learning (ML) based prediction model considering the pharmacophoric features of both NEP and DPP-4. The model was tested against an array of in-house developed and newly designed and synthesized NCEs as training sets with the reported inhibitors against the enzyme. The work was further validated and standardized with molecular docking and dynamics studies and corroborated with numerous biological studies. The cumulative analysis yielded **1a** and **1f** as the best lead molecules with potent dual inhibition of NEP and DPP-4 with anti-diabetic potential.



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sciforum-152090: Molecular docking study of hydroxyquinolone derivatives as COX enzyme inhibitors

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Cyclooxygenases (COXs) are essential enzymes involved in the biosynthesis of prostanoids, which play key roles in inflammation and various physiological processes. COX-1 is responsible for maintaining normal homeostatic functions, whereas COX-2 is inducible and primarily expressed during inflammatory and pathological conditions. Nonsteroidal anti-inflammatory drugs (NSAIDs) exert their effects by inhibiting COX enzymes; however, their non-selective action often leads to adverse effects, prompting the development of selective COX-2 inhibitors.

Heterocyclic compounds, particularly hydroxyquinolin-2-ones, have attracted significant attention due to their diverse pharmacological activities, including antibacterial, anticancer, and anti-inflammatory properties. In this study, we focused on designing and evaluating in silico of hydroxyquinolin-2-one derivatives as potential therapeutic agents targeting inflammation and infectious diseases.

Molecular docking studies were carried out on the synthesized hydroxyquinolin-2-one derivatives to assess their binding affinity toward the COX enzyme. The results demonstrated promising docking scores for all derivatives, indicating a strong potential for COX inhibition. Compounds with the highest docking scores formed significant interactions with key residues in the COX active site, primarily through hydrogen bonding and other stabilizing interactions. These interactions were facilitated by the presence of carbonyl and hydroxyl groups in the ligand structures, highlighting their crucial role in enhancing binding affinity and stability within the enzyme's active site.



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sciforum-150383: New potential inhibitors molecules of the envelope protein from dengue virus type 2

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Background. By 2024, 14.1 million cases of dengue were reported around the world, folding the amount of 2023. Dengue is an orphan disease caused by the dengue virus (DENV), and it's transmitted by mosquitoes such as *Aedes aegypti*, which has one of the highest reproductive rates and is more susceptible to the DENV-2 serotype. Scientific studies indicate that the envelope protein (EP) could be inhibited avoiding the viral fusion and interrupting the replication.

Method. EP was downloaded from PDB (1OKE code) and processed using PyMOL software. The scaffold was selected by searching for active chemical structures in ChEMBL from a study of 163 molecules. Molecular docking was performed using Autodock-Vina 1.1.2. The molecules with the highest activity were 36 and 136. In molecular dynamics the molecule 136 exhibited a better affinity, binding the amino acid THR48 of EP through the pharmacophore alpha-ethylidene thiohydantoin. One thousand one hundred thirty three bioisosteres were performed using alpha-ethylidene thiohydantoin scaffold with the Zinc 20 database. The bioisosteres were bring under molecular docking and four were selected.

Results. Molecules 1104, 1101, 1154, and 872 were found with better affinity than 136, they put through to molecular docking using Autodock Vina 1.1.2. SAR analysis of molecule 1104 show greater activity due to the ketone group, which influences the coplanarity of the heterocyclic cyclopentane, making better use of the pocket of the EP catalytic site and stabilizing by forming hydrogen bonds with AL50.

Conclusions. Four novel compounds of promising activity against envelope protein of dengue virus type 2 where found.



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sciforum-151985: Next-Generation Selenium Compounds as Potential Disease-Modifying Agents in Alzheimer's

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Alzheimer's disease (AD) is the most prevalent neurodegenerative disorder and the sixth leading cause of death worldwide, with cases continuing to rise at an alarming rate and imposing major social, economic, and healthcare burdens. Despite over a century of research, effective disease-modifying therapies remain elusive. Several pathogenic mechanisms—including amyloid- β (A β) aggregation, tau hyperphosphorylation, acetylcholine deficiency, and oxidative stress—have been explored to elucidate AD progression. Among these, targeting the A β cascade has emerged as a particularly promising therapeutic strategy, especially in the early stages of the disease. Consequently, the development of small molecules capable of modulating amyloid aggregation represents a critical avenue for advancing novel AD treatments.

In this work, a novel library of *N*-benzylphenoselenazine (PSZ) derivatives (8a–j) was designed, synthesized, and systematically evaluated for their ability to inhibit A β 40 aggregation, a central hallmark of AD pathology. Structure–activity relationship (SAR) studies using thioflavin T fluorescence assays demonstrated significant inhibition across the series, ranging from 26.0% to 86.4%. Compounds 8i and 8j exhibited particularly strong effects, reducing aggregation by ~75% and 86% at 25 μ M, respectively—comparable to standard reference inhibitors resveratrol (~85%) and methylene blue (~96%). Transmission electron microscopy (TEM) confirmed their ability to disrupt A β 40 fibril formation, while computational docking studies indicated favorable interactions with the hydrophobic KLVFFA motif of the A β 40 dimer, stabilizing its structure and impeding further aggregation.

These findings establish *N*-benzylphenoselenazines as promising lead candidates for therapeutic development aimed at the amyloid cascade. By combining synthetic design, biological evaluation, and computational modeling, this study underscores the potential of selenium-based scaffolds as innovative agents for addressing the unmet therapeutic challenges of Alzheimer's disease.



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sciforum-151504: Ornithine Derivatives of Salicylamide with Cytotoxic Potential against A549 Human Lung Carcinoma Cells

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Peptidomimetics represent a promising class of biologically active compounds with broad therapeutic potential. In general, peptidomimetics mimic the functions of natural peptides in the human body while overcoming their inherent limitations (e.g., low stability or poor bioavailability), thus finding application in the treatment of a wide range of diseases. This study focuses on the synthesis and cytotoxic properties of short original ornithine-based peptidomimetics derived from substituted *O*-benzyl-protected salicylic acid (salicylamides), where L-ornithine is further modified with various aromatic amines, and on the evaluation of their biological activity against the A549 human lung carcinoma cell line. Salicylic acid-based peptidomimetics have previously been synthesized by our research group, demonstrating both anticancer and antimicrobial activity. Ornithine-containing peptidomimetics represent synthetic precursors leading to arginine-based peptidomimetics. Arginine peptidomimetics exhibit a broad spectrum of biological activities, including antimicrobial, antiviral, antifungal, anticancer (e.g., cilengitide), and activity against cardiovascular (e.g., argatroban) and neurodegenerative diseases. The A549 cell line is a standard *in vitro* model for testing novel candidate anticancer agents against non-small cell lung carcinoma (NSCLC), the most prevalent clinical form of lung cancer. In this study, short ornithine-derived and specific salicylamide derivatives with potential biological activity against the A549 cell line were prepared. The peptidomimetic backbone was synthesized via Steglich amidation, and the side chain was modified. The anticancer activity of the synthesized compounds was determined *in vitro* against the A549 cell line, for final compounds as well as for their precursors. The presentation will address the structure–activity relationships observed in this series.



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sciforum-152201: Preliminary Evaluation of New Benzenesulfonamides as Anticancer Agents Against DU-145 Prostate Cancer Cells

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Introduction: The unfolded protein response (UPR), a critical pathway managing endoplasmic reticulum (ER) stress, could be hijacked by malignant cancer cells to promote survival, angiogenesis, and metastasis. Its central sensor, IRE1 α , has emerged as a key regulator of cancer cell adaptation and therapeutic resistance. Prostate cancer, the most common malignancy in European men, remains a significant clinical challenge, particularly upon progression to therapy-refractory forms, highlighting the urgent need for novel therapeutic strategies. Pharmacological modulation of IRE1 α signaling offers a promising avenue to disrupt cancer cell homeostasis and enhance treatment efficacy.

Methods: In this work, we designed and synthesized a novel series of twelve benzenesulfonamide derivatives (APS) featuring a polynitrogen scaffold, with the goal of targeting the UPR. The compounds' cytotoxic potential was determined in the DU-145 prostate cancer cells by XTT assay after 24 and 48 hours of exposure.

Results: The screening identified two lead compounds with distinct activity profiles. APS 600 was the most potent agent at 24 hours (IC₅₀ = 10.23 μ M), while APS 597 demonstrated superior activity after 48 hours (IC₅₀ = 14.67 μ M). A preliminary structure-activity relationship analysis suggests that the cytotoxic effect could be influenced by the substitution pattern of the 1,2,4-triazole moiety.

Conclusions: These findings designate APS 597 and APS 600 as valuable lead candidates warranting continued development. The study provides compelling support for mechanistic follow-up to determine their mode of action within IRE1 α -regulated signaling pathways. Further refinement of this scaffold has the potential to generate highly selective ER stress modulators with improved therapeutic specificity and reduced off-target toxicity.



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sciforum-142579: QSAR Modelling of Ferulic-Acid Derivatives to Support the Design of Brain-Penetrant Acetylcholinesterase Inhibitors for Alzheimer's Therapy

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Background: Acetylcholinesterase (AChE) remains a clinically validated target for symptomatic treatment of Alzheimer's disease (AD), yet current inhibitors display only moderate brain penetration and dose-limiting adverse effects. Ferulic acid (FA) exhibits neuroprotective properties and weak AChE inhibition, encouraging structural optimisation. **Methods:** The chemical structures and Ellman-assay IC_{50} values for twenty FA derivatives were taken as reported in a previous external study. Three-dimensional geometries were energy-minimised (MM⁺→PM3) and analysed in Dragon 7 to generate 4,885 molecular descriptors. After variance/multicollinearity filtering, 918 descriptors remained. Stepwise feature selection identified four informative variables—nCL, SpMax2_Bh(p), Mor16s, SpMax7_Bh(s)—capturing halogen content, electronic distribution, and 3-D shape. An artificial neural network (MLP 4-8-1, BFGS optimisation) was trained on a 14-compound set and validated by leave-one-out cross-validation and an external three-compound test set. **Results:** The model reproduced experimental data with $R^2 = 0.959$, $Q^2 = 0.956$ and MAE = 1.43 μ M; external prediction yielded $R^2 = 0.927$. Sensitivity analysis revealed SpMax2_Bh(p) as the principal driver of potency, while nCL highlighted the favourable impact of chloro-substitution. **Conclusions:** A concise ANN-QSAR model delivers accurate, mechanism-based predictions of AChE inhibition for FA derivatives and offers clear design rules—enhanced π -cloud polarisability and selective halogenation—for the next generation of brain-penetrant AChE inhibitors. The workflow shortens the discovery timeline for AD therapeutics and can be expanded to larger libraries and multi-target optimisation.



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sciforum-152257: Quinoline-acylhydrazone hybrids as potential agents against chikungunya virus: Synthesis, Biological Screening and in silico studies

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Chikungunya fever is an arboviral disease that manifests as an acute illness, whose symptoms include fever, rash, and severe, debilitating arthralgia. Despite its low mortality rate, the disease can present severe forms, especially in at-risk groups such as neonates, the elderly, and individuals with comorbidities. In the search for new drugs to treat the disease, our group has been exploring N-acylhydrazone as a privileged structure in medicinal chemistry. Quinolines and their chemical derivatives have been assayed against a diverse panel of viruses with promising results. In this project, we hybridised the N-acylhydrazone with the 7-Chloroquinoline ring to produce a series of 33 compounds, which were synthesised, purified and subjected to antiviral activity assays to determine their Half Maximal Effective Concentration (EC₅₀) against the virus and the Cytotoxic Concentrations 50% (CC₅₀) against the host cells (Dose-response curves with 10 dilution points). Three compound exhibited EC₅₀ values lower than 10 µM: GPQF-8Q33 (EC₅₀: 0.56 µM; SI: 77.7), GPQF-8Q28 (EC₅₀: 1.26 µM; SI: 79.4) and GPQF-8Q34 (EC₅₀: 9.08 µM; SI: 40). These compounds were *in silico* docked into the NsP2 protease, a potential target of the virus and exhibited a panel of interaction consistent with molecular recognition. Molecular dynamics simulation corroborates the stability of the complexes as well as indicates which interactions are mostly predominant in recognition binding. Synthesis was accomplished by simple coupling of aldehydes with quinoline-hydrazines, in mild conditions (EtOH/AcOH, 80°C, 24h). Docking studies were performed after a cross-docking assay, using Autodock software and considering a GRID centred at Trp1084 and with dimensions of 54x54x54 points. Molecular dynamics simulation of 400 ns was performed at 300°C, considering steps of 1 fs each. Chamm-gui web-based software and Gromacs were employed in these studies.



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sciforum-152330: Ru(II) and Pt(II) Based Phosphorescent Biosensors and Phosphorescence Optical Respirometry in Antibacterial Activity Studies of Co(III) Complexes with Diamine Chelate Ligands

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Introduction:

The urgent demand for new antimicrobial strategies has highlighted transition metal complexes as promising therapeutic candidates. Among them, Co(III) complexes with diamine chelate ligands exhibit notable stability and biomolecular affinity. To elucidate their antimicrobial activity and mode of action, phosphorescent Ru(II)- and Pt(II)-based probes are particularly advantageous due to their oxygen-sensitive phosphorescence. Phosphorescence optical respirometry (POR) enables real-time monitoring of microbial respiration, providing a sensitive measure of metabolic inhibition induced by metal complexes.

Materials and Methods:

Co(III)-diamine complexes were synthesized and characterized by elemental analysis, an ATR technique, and a scan method. Their antimicrobial properties were examined against representative gram-positive (*Staphylococcus aureus*, *Staphylococcus epidermidis*) and gram-negative (*Escherichia coli*, *Pseudomonas aeruginosa*) reference and clinical bacterial strains. Ru(II) and Pt(II) phosphorescent probes were employed in POR assays to monitor oxygen consumption as a marker of cellular respiration.

Results:

The Co(III) complexes displayed strain-dependent antimicrobial effects, with more pronounced activity against gram-positive bacteria. POR measurements revealed a dose-dependent suppression of microbial respiration, consistent with metabolic inhibition. Changes in phosphorescence lifetimes of Ru(II) and Pt(II) probes confirmed oxygen depletion dynamics and allowed kinetic profiling of bacterial response to the complexes.

Conclusions:

Ru(II) and Pt(II) phosphorescent biosensors, applied through phosphorescence optical respirometry, provide a robust platform for investigating the antimicrobial activity of Co(III)-diamine complexes, as well as other antimicrobial compounds. This method not only enables sensitive detection of respiratory inhibition but also permits the determination of viable aerobic microbial cell counts through analysis of the phosphorescence value and offers mechanistic insights into the biological action of metal-based therapeutics and. These findings establish a foundation for further development the PRO method to investigate the interactions of antibiotics and antimycotics with newly developed metal complex-derived antimicrobial agents targeting microorganisms.



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sciforum-129128: Search and creation of new biologically active organic substances based on 6-(5-mercapto-4-phenyl-4*H*-1,2,4-triazol-3-yl)pyrimidine-2,4(1*H*,3*H*)-dione

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The search and development of new biologically active organic compounds remains a cornerstone of modern medicinal chemistry. Among the promising scaffolds, 6-(5-mercapto-4-phenyl-4*H*-1,2,4-triazol-3-yl)pyrimidine-2,4(1*H*,3*H*)-dione stands out due to its unique combination of heterocyclic moieties. This scaffold not only incorporates the biologically significant 1,2,4-triazole ring—a well-known pharmacophore with antimicrobial, antioxidant, and anti-inflammatory properties—but also integrates the pyrimidine-2,4-dione fragment, structurally related to vitamin B13 (orotic acid), which is essential for nucleic acid biosynthesis. The synergy between these two fragments opens up new avenues for designing compounds with enhanced pharmacological profiles.

In this study, we synthesized a series of novel derivatives based on the core 6-(5-mercapto-4-phenyl-4*H*-1,2,4-triazol-3-yl)pyrimidine-2,4-dione scaffold by introducing various substituents via *S*-alkylation and *S*-arylation reactions, aiming to modulate lipophilicity and electronic properties. These modifications are expected to influence the compounds' bioavailability and interactions with biological targets. The synthesized derivatives were characterized by spectroscopic techniques, including NMR, to confirm their structures. Preliminary biological evaluations revealed that several compounds exhibited significant antimicrobial activity against both Gram-positive and Gram-negative bacteria, along with notable antioxidant potential in standard DPPH assays.

These results suggest that hybrid molecules combining the triazole-thiol moiety and the vitamin B13-derived pyrimidine-dione core represent a promising class of compounds for further pharmacological development. Ongoing studies are focused on detailed pharmacological profiling, mechanism-of-action investigations, and structure-activity relationship (SAR) analyses to optimize their biological efficacy and safety. The potential applications of these derivatives may extend to antimicrobial therapy, anti-inflammatory treatment, and antioxidant interventions, paving the way for innovative therapeutic agents.



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sciforum-151812: Selenocyanate Derivatives as Acetylcholinesterase Inhibitors: Potential Therapeutic Agents for Alzheimer's Disease

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Acetylcholinesterase (AChE) plays a key role in the pathophysiology of Alzheimer's disease (AD) by promoting excessive hydrolysis of acetylcholine, leading to a marked cholinergic deficit. This increased enzymatic activity is directly linked to cognitive decline in AD, making AChE inhibition a cornerstone of current symptomatic treatment strategies [1]. In this context, organocalcogen compounds, particularly selenium derivatives, have gained attention due to their redox, antioxidant, and enzyme-modulating properties, as well as their versatility in coordinating with biomolecules [2,3]. In this study, the synthesis of two distinct classes of SeCN-containing derivatives, alkyl and aryl, was performed. The alkyl derivatives were obtained via established procedures involving bimolecular nucleophilic substitution reactions. In contrast, the aryl derivatives were synthesized through aromatic nucleophilic substitution, initiated by diazonium salt formation. As a result, a series of five compounds was successfully prepared and subsequently subjected to AChE inhibition assays *in vitro* using samples of mouse brains. Biological activity was assessed through a colorimetric assay using acetylthiocholine as substrate. Analysis of Variance (ANOVA) revealed a significant difference among groups [$F_{(26,52)} = 34.97$; $p0.0001$]. Aromatic derivatives showed inhibitory activity from 15 μM , while aliphatic analogues were active from 10 μM . Rivastigmine (200 μM , a clinical AChE inhibitor) was used as positive control. The results demonstrate that selenocyanates present relevant inhibitory activity against cerebral AChE *in vitro* and stand out as promising candidates for the development of novel therapeutic approaches for AD.



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sciforum-152320: Selenotetrazole Derivatives as Selective Antioxidants with Redox-Modulating Potential

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Oxidative stress plays a central role in the pathogenesis of neurodegenerative, cardiovascular, and inflammatory disorders, as well as cancer. In this sense, the discovery of novel antioxidant agents has a critical priority in medicinal chemistry. Organoselenium derivatives stand out in this context for their ability to modulate redox processes, frequently mimicking the activity of glutathione peroxidase (GPx). At the same time, the tetrazole nucleus functions as a bioisosteric moiety, widely employed in clinically approved drugs due to its favorable pharmacokinetic and pharmacodynamic properties. The strategic combination of these two pharmacophoric elements results in selenotetrazoles, molecules with promising biological potential and new perspectives for therapeutic development. The compounds were obtained via [3+2] cycloaddition between SeCN-containing precursors and sodium azide. In this work, the antioxidant activity of the newly synthesized selenotetrazoles was evaluated through radical scavenging assays (ABTS•+ and DPPH•) to investigate their redox-modulating potential. In the ABTS•+ assay, which measures the ability of molecules to neutralize radicals in aqueous medium, ethyl 3-(1H-tetrazol-5-yl)selanyl benzoate and ethyl 4-(1H-tetrazol-5-yl)selanyl benzoate at 200 µM showed significant antioxidant activity, comparable to ascorbic acid (positive control, 25 µM). Conversely, in the DPPH• assay, which evaluates electron transfer in apolar medium, the compounds showed no significant activity. This selectivity suggests that their antioxidant effect is not based on electron transfer in nonpolar systems, but rather occurs in aqueous environments, consistent with a GPx-like mechanism. In conclusion, the synthesized selenotetrazoles present selective antioxidant activity, redox stability and multitarget potential, consolidating them as promising scaffolds for the development of antioxidant, anti-inflammatory, neuroprotective and/or anticancer agents.



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sciforum-152096: Some cytotoxic effects of 3-amino derivatives of pentacyclic triterpenoids towards cancer cells

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Due to their broad-spectrum bioactivities and compliance with directed functionalization, pentacyclic triterpenoids (PCTs) are considered a potent molecular platform for novel drug development. Cytotoxic and pro-apoptotic activities of PCTs involving different specific mechanisms are of substantial interest in preferable targeting cancer cells. Replacement of C-3 hydroxyl group of ursolic acid by the nitrogen-containing group was earlier found to promote cytotoxicity of the triterpenoid. In this work, we studied and compared cytotoxicity of pre-synthesized and characterized lupane triterpenoid derivatives containing hydroxyl, amino or carboxymethyl amine groups at C-3 position. According to resazurin assay upon 3-day culture, the modified PCT showed increased inhibitory effect on viability of breast and prostate cancer cells (MCF-7 and PC-3 lines) with half-maximum inhibitory concentrations in the micromolar range. According to flow cytometry analysis with reactive oxygen species (ROS)-specific fluorescent probes, the synthesized compounds exhibited modulating concentration-dependent effects on cytoplasm and mitochondrial ROS levels; the most active derivative caused significant ROS overproduction, which probably underlies its cytotoxic effect. The obtained results contribute to the design of PCT derivatives with potential anticancer properties and encourage further investigation of the compounds. The study was supported by the Subsidy Allocated to Kazan Federal University for the State Assignment in the Sphere of Scientific Activities (project FZSM-2025-0002).



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sciforum-151617: Stimulation of thyroid hormone synthesis by ethyl-2-(4-(4-(5-amino-6-(tert-butylcarbamoyl)-2-(methylthio)thieno[2,3-d]-pyrimidin-4-yl)phenyl)-1H-1,2,3-triazol-1-yl) acetate (TPY3m) and thyroliberin in aging normal and obese rats

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Obesity is often accompanied by hypothyroidism, the severity of which worsens with aging, which may be due to a decrease in the sensitivity of thyrocytes to thyroid-stimulating hormone (TSH). Thyroid hormone replacement therapy is usually used to compensate for thyroid hormone (TH) deficiency, but it has significant limitations. Allosteric TSH receptor agonists, including our developed TPY3m, a thieno[2,3-d]-pyrimidine derivative, may be proposed as an alternative. The aim of this study was to compare the effects of TPY3m and thyroliberin (TRH) on TH and TSH levels in the blood of aging rats, including obese ones. Male rats (18-month-old) were administered TPY3m (20 mg/kg, i.p.) and TRH (100 µg/rat, intranasally). Obesity was induced by a 12-week high-fat diet (OB). Hormone levels (fT4, fT3, tT3, TSH) were assessed using ELISA, calculating the index of peripheral conversion ([fT3]/[fT4], IPC) and the integral thyroid index ([fT3]+[fT4]/[TSH], ITI). In aging obese rats, the fT3 level, ICI and ITI were reduced. Treatment of the OB group with TRH increased TSH and fT4 levels, but to a lesser extent than in the control. The ITI index remained reduced. TPY3m increased fT4 and fT3 levels in the OB and control groups, but, unlike TRH, did not affect the TSH level, increased the ITI, and normalized the ICI. Thus, TPY3m similarly stimulated TH production in aging rats with and without obesity, whereas the stimulatory effects of TRH were reduced in obesity, indicating that the sensitivity of the TSH receptor to allosteric agonists is preserved in aging and obesity.

The study was supported by the RSF (No 19-75-20122).



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sciforum-151341: Structure-Based Design of Hybrid Molecules Exhibiting Dual SGLT2 and AT1 Inhibition for Cardiorenal Protection: A Computational and Medicinal Chemistry Strategy

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Combination therapy for metabolic diseases has traditionally been associated with an increased risk of chronic kidney disease (CKD). However, the co-administration of sodium-glucose cotransporter 2 (SGLT2) inhibitors and angiotensin II type I receptor antagonist (AT1) have demonstrated a protective effect against CKD progression. To build upon this therapeutic potential, the present study introduces an *in silico* design of a hybrid molecule as an innovative pharmacological strategy.

This approach integrates the key pharmacophores of empagliflozin (SGLT2 inhibitor) and telmisartan (ARB) into a single molecular entity, aiming to enhance nephroprotective synergy while streamlining the treatment regimen. The computational workflow began with the generation of a bioisostere library comprising 2017 compounds sourced from the Zinc20 database. Molecular docking simulations were conducted using the VINA 1.1.2 algorithm to assess binding affinity and stability toward both target receptors: SGLT2 (PDB: 7VSI) and AT1 (PDB: 4ZUD).

The lead candidate was identified based on its optimal Gibbs free energy values for both receptors and its favorable pharmacokinetic and safety profile, as predicted by ADMETlab 3.0. Visualization and analysis of docking interactions were performed using PyMOL and Discovery Studio.

This study not only confirms the feasibility of combining two complementary mechanisms of action within a single compound but also proposes a promising candidate for subsequent development stages, including chemical synthesis and preclinical evaluation (*in vitro* and *in vivo*). These findings lay the groundwork for a new generation of targeted therapies that are safer and more effective in protecting kidney and cardiovascular health.



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sciforum-152291: Synthesis and evaluation of anticancer activity of pyrrolo[3,4-d]isoxazoles against tumor cell lines

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Oncological diseases represent a major global health challenge and are the second leading cause of mortality. The discovery of novel chemotherapeutic agents with improved efficacy and safety profiles remains a critical objective in medicinal chemistry. In this pursuit, heterocyclic compounds serve as privileged structures in drug design. Isoxazole derivatives, in particular, are recognized as a prime scaffold due to their remarkable ability to interact with diverse biological targets, demonstrating a broad spectrum of pharmacological activities.

This work focuses on the design, synthesis, and biological evaluation of a new series of heterocyclic compounds incorporating the synthetically versatile pyrrolo[3,4-d]isoxazole framework. The synthesized novel derivatives were screened for their *in vitro* antiproliferative activity against three human cancer cell lines: cervical carcinoma (HeLa), erythroleukemia (K-562), and melanoma (Sk-mel-2). The results revealed that several adducts exhibited significant cytotoxic effects, with half-maximal inhibitory concentration (IC_{50}) values as potent as 15 μ g/mL.

To gain insight into the potential mechanism of action, a confocal microscopy analysis was conducted. Treatment with the active compounds induced pronounced cytoskeletal alterations, specifically a diffuse redistribution of granular actin within the cytoplasm concomitant with the disappearance of structured actin filaments. A notable reduction in filopodia-like membrane protrusions was also observed. These findings collectively substantiate the promising antitumor potential of the synthesized pyrrolo[3,4-d]isoxazole derivatives, warranting further investigation into their therapeutic applications.



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sciforum-149203: Synthesis of 2-(4-isobutylphenyl)-N-(naphthalen-1-yl)propanamide

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The development of hybrid molecules that integrate distinct pharmacophores represents a valuable strategy in medicinal chemistry to enhance therapeutic potential. In this work, we describe the synthesis of 2-(4-isobutylphenyl)-N-(naphthalen-1-yl)propanamide, a novel amide derivative that combines the structural features of ibuprofen, a prototypical nonsteroidal anti-inflammatory drug (NSAID), with naphthalen-1-amine, an aromatic amine of pharmacological interest. The target compound was obtained via a single-step synthetic strategy employing dicyclohexylcarbodiimide (DCC) as a coupling reagent. Specifically, the carboxylic acid functionality of ibuprofen was activated in situ with DCC, enabling nucleophilic substitution by naphthalen-1-amine to afford the desired amide. The product was purified by recrystallization and chromatographic techniques, and its structure was confirmed using FTIR, ¹H NMR, ¹³C NMR, and mass spectrometry.

This hybridization approach was designed to merge the anti-inflammatory pharmacophore of ibuprofen, known for cyclooxygenase (COX) inhibition, with the lipophilic naphthylamine scaffold, which could modulate binding interactions or pharmacokinetic behavior. The straightforward use of DCC-mediated amide bond formation demonstrates the efficiency of this method in generating novel derivatives without the need for multistep activation or protection strategies. While the current study emphasizes the synthesis and characterization of the compound, future investigations will explore its biological activity and potential improvements in anti-inflammatory efficacy compared to the parent drug.



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sciforum-151054: Synthesis of new quinoline analogs of selected neuroleptics

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Introduction Neuroleptics are used as psychotropic medication for treatment of psychosis, schizophrenia, bipolar disorder, apathy and neurosis. The latest research on their biological activity shows their new activities including anticancer against brain, lung, breast, liver and colon cancer, antiviral against SARS-CoV and suppression of infections caused by dengue virus. Neuroleptics such as fluphenazine, triflupromazine and trifluoperazine were the research subject. The aim of the study was to synthesize new quinoline analogs of selected neuroleptics as new drugs' candidates with more beneficial ADMET profiles.

Methods To synthesize new quinoline analogs, 6H-8-trifluoromethylquinobenzothiazine was synthesized by the reaction of 2-amino-4-trifluoromethylthiophenol with 3-bromo-2-chloroquinoline. After synthesizing 6H-8-trifluoromethylquinobenzothiazine its structure was confirmed by spectroscopic methods. Afterwards 6H-8-trifluoromethylquinobenzothiazine was used as a substrate to obtain new quinoline analogs with pharmacophore dialkylaminoalkyl substituents. The structure of each one of newly synthesized compounds was confirmed by the use of spectroscopic methods such as ¹H NMR, ¹³C NMR and ESI HR MS. All synthesized compounds were studied for anticancer activity against three human cancer cell lines: breast (MDA-MB-231), pancreatic (Mia-PaCa-2) and lung (A-549). Doxorubicin and cisplatin were used as reference drug. Human keratinocyte cell line (HaCaT) was used as healthy cells.

Results The research carried out allowed to synthesize 6H-8-trifluoromethylquinobenzothiazine and to obtain new quinoline analogs with pharmacophore dialkylaminoalkyl substituents. Currently, eleven new quinoline analogs were synthesized. The study for anticancer activity allowed to determine concentration of new compounds required for 50% inhibition of three human cancer cell lines.

Conclusions The method chosen to synthesize new quinoline analogs was effective and allowed eleven new compounds to be obtained. The study for anticancer activity against three human cancer cell lines concludes that there are three compounds that show the most promising anticancer activity (IC₅₀ 5.5 μM).



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sciforum-151716: Synthesis, crystallographic structure, and antibacterial activity of new pyrene-based hydrazones

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Hydrazones are compounds that exhibit a broad range of biological activities, including anticancer, antifungal, antimicrobial, anti-inflammatory, anticonvulsant properties. On the other hand, pyrene is a highly conjugated polycyclic aromatic hydrocarbon that has been used in antimicrobial and bioimaging studies, showing activity against wild-type bacteria and fungal species. In this work, we synthesized new hydrazones derived from 1-pyrenecarboxaldehyde (**1**) with various *para*-substituted phenylhydrazines (**2a-d**) bearing electron-withdrawing groups such as fluorine, chlorine, and bromine, since these halogens are associated with enhanced biological activity and improved permeability. Additionally, an electron-donating group (4-OCH₃) was included due to its prominence in several known derivatives with anticancer activity.

For the synthesis of hydrazones **3a-d**, a mixture of 1-pyrenecarboxaldehyde (**1**) and *p*-phenylhydrazines (**a**: 4-Cl, **b**: 4-Br, **c**: 4-CF₃, **d**: 4-OCH₃) was stirred in ethanol at 80 °C, yielding the desired products (**3a-d**) in 73-90%, which were characterized by IR spectroscopy, ¹H and ¹³C NMR, mass spectrometry, and single-crystal X-ray diffraction of **3d**, obtained by slow evaporation from ethanol. Hydrazones **3a-d** exhibited bacteriostatic activity against *Mycobacterium tuberculosis*, and compound **3d** was active with a MIC = 40 µg/mL. Moreover, all compounds showed anticancer activity against breast cancer cells (MCF-7) with and IC₅₀ value 6.25 µg/mL, and compound **3d** (4-OCH₃) exhibits the highest inhibitory activity against cervical cancer cells (Hep-2) with an IC₅₀ of 67.2 µg/mL. Molecular docking studies were performed using the binding pocket of PDB: 2OZ5. The protein-ligand complex of compound **3d** exhibited interactions with catalytic residues Met146, Arg230, and Met226.



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sciforum-152215: The Concept of Development and Creation of Original Metabolitotropic Endotheliotropic Drugs with Cardio- and Neuroprotective Effects Based on 3-Methyl-1,2,4-triazolyl-5-thiocarboxylic Acids. A Promising Example of Angiolin

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Endothelial dysfunction (ED) is currently recognized as a key pathogenic factor in the development of cardiovascular diseases. Reduced bioavailability of nitric oxide (NO), increased oxidative and nitrosative stress, and disruption of redox homeostasis contribute to vascular endothelial damage, leading to ischemic, hypertensive, and neurodegenerative conditions. Currently, there is no pharmacotherapy specifically targeting ED, highlighting the urgent need for novel therapeutic agents with endothelioprotective properties.

This study highlights the rationale and experimental basis for the creation of a new class of pharmacological agents—endothelioprotectors. Particular focus is given to a new compound, Angiolin (S)-2,6-diaminohexanoic acid 3-methyl-1,2,4-triazolyl-5-thioacetate, designed as an endothelioprotector with neuro- and cardioprotective capabilities. Structurally combining L-lysine and thiotriazoline fragments, Angiolin demonstrates a wide spectrum of pharmacological activities, including endothelioprotective, cardioprotective, neuroprotective, anti-ischemic, antioxidant, and anti-inflammatory effects.

Preclinical studies have shown that Angiolin enhances NO bioavailability, protects endothelial cells, preserves mitochondrial function, activates the glutathione system, and prevents oxidative damage in ischemic tissues. Furthermore, Angiolin improves cerebral and cardiac hemodynamics, promotes ATP production via the malate-aspartate shuttle, and modulates GABAergic neuroprotection by increasing pipecolic acid levels.

Toxicological assessment classifies Angiolin as a substance of low toxicity (Class VI), and Phase I clinical trials conducted with the approval of the Ministry of Health of Ukraine confirmed its safety profile. The compound represents a promising therapeutic strategy for complex treatment of chronic cerebral ischemia, myocardial infarction, heart failure, and prenatal hypoxia, offering advantages over current metabolitotropic drugs such as meldonium, piracetam, and trimetazidine.

In conclusion, Angiolin is a novel pharmacological agent with targeted endothelioprotective action and broad metabolic, cardio-, and neuroprotective potential, warranting further clinical investigation.



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sciforum-152164: The Effect of a Metal Atom on the Photochemical and Photobiological Properties of Porphyrazine as an Agent for PDT

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Modification of the known structures of photosensitizers (PS) in purpose to improve their properties is an important direction in the development of new agents for photodynamic therapy (PDT). Among the approaches, the incorporation of different metals in the structure of the PS molecule can be distinguished. In this research, we investigated the photophysichemic and photobiological properties of tetrakis(3-methyl-1-phenyl-pyrazole-4-yl)-tetracyanoporphyrazine (PzPyr) and its metal complexes containing iron and palladium cations in the center of the macrocycle.

Two absorption bands were observed for the studied compounds: in the short-wavelength (Soret band) and long-wavelength (Q-band) regions, and fluorescence in the red region of the spectrum with peak at 620–650 nm. The compounds demonstrated a significant increase in fluorescence intensity in a more viscous medium, which suggests that they belong to the class of fluorescent molecular rotors.

We did not observe any visible differences in the accumulation dynamics for PzPyr and FePzPyr – the maximum accumulation occurred 1 hour after the start of incubation, indicating a high rate of uptake by A431 cells. At the same time, PdPzPyr showed a longer accumulation time of more than 5 hours.

Evaluation of the cytotoxicity of the compounds showed that they exhibit a low level of dark toxicity, while maintaining visible photodynamic activity A431 cells. The addition of a metal cation resulted in a significant increase in the photodynamic index compared to the free base. Inhibitory analysis demonstrated that FePzPyr and PdPzPyr are able to induce cell death along the immunogenic pathway.

Analysis of the compounds has shown that they can be used as potential drugs, and the addition of a metal atom opens up broad prospects for improving the effectiveness of PDT, for example, by activating immunogenic cell death pathways.

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sciforum-151906: Three-Dimensional Shape Similarity Approach for the Discovery of IL-1R1 Receptor Inhibitors

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Interleukin-1 β (IL-1 β) is a prototypical cytokine of the IL-1 family that regulates innate and adaptive immunity. Its cognate receptor, interleukin-1 receptor type 1 (IL-1R1), is therefore a tractable target for anti-inflammatory drug discovery. The peptide antagonist AF10847 binds IL-1R1 and disrupts the IL-1 β /IL-1R1 protein-protein interface, validating the receptor's druggability. However, its peptidic nature entails poor oral bioavailability and unfavorable developability. This study aimed to discover non-peptidic small molecules capable of inhibiting IL-1R1 using a 3D shape-similarity strategy anchored on AF10847. The IL-1R1/AF10847 co-crystal structure was prepared for modeling, and the binding pocket was delineated using FPocket, DoGSiteScorer, and DeepSite. *In silico* alanine scanning of the complex identified interaction "hot spots" at the protein-protein interface. Following comprehensive conformer enumeration of AF10847, a ROCS query capturing its molecular envelope and salient pharmacophoric features was constructed and deployed to virtually screen large purchasable libraries (Enamine, ChemDiv, Asinex and NCI Open Database). Candidates were ranked by Tanimoto similarity score and lightly filtered for drug-likeness prior to structure-based triage. Top-ranked molecules underwent ensemble molecular docking into multiple IL-1R1 conformations to accommodate receptor flexibility, with poses assessed by consensus scoring and interaction-fingerprint analysis for consistency with the AF10847 recognition pattern. Short all-atom molecular-dynamics simulations were then performed to evaluate pose stability via heavy-atom RMSD and hydrogen-bond occupancy and to obtain qualitative affinity estimates using trajectory-averaged metrics. This computational cascade identified several chemically diverse small-molecule candidates predicted to engage IL-1R1 in persistent, well-packed poses with favorable interaction networks. These *in silico* hits constitute tractable starting points for experimental validation, including biochemical binding assays and cellular readouts of IL-1 β signaling, orthogonal selectivity counterscreens early ADMET profiling to guide medicinal-chemistry optimization toward orally available IL-1R1 modulators.



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sciforum-152247: Unravelling the Quinoline Encompassing Pyrimidin-2-thione as a Acetylcholinesterase Inhibitors: Synthesis, Spectral analysis, Drug likeness predictions, *In vitro*, and *In silico* Molecular Modelling studies

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To develop pharmacologically active molecules, a series of analogues of 3-(1,2-dihydro-6-substituted phenyl-2-thioxopyrimidin-4-yl)-1-methylquinolin-2(1H)-one (compounds 4a-j) were synthesized through condensation and ring-closure reactions, yielding novel pyrimidine derivatives. These newly synthesized 2-quinolone-linked pyrimidin-2-thiol analogues were structurally characterized using various spectroscopic techniques. The compounds were evaluated for their antioxidant activity using the DPPH (2,2-diphenyl-1-picrylhydrazyl) assay, and for anti-Alzheimer potential through acetylcholinesterase (AChE) inhibition, assessed via Ellman's method. Among the series, compounds 4c and 4e, containing electron-donating groups on the phenyl ring, showed excellent radical scavenging activity. In AChE inhibition studies, compound 4c [3-(1,2-dihydro-2-thioxo-6-p-tolylpyrimidin-4-yl)-1-methylquinolin-2(1H)-one] exhibited notable inhibitory activity, likely due to the influence of the p-tolyl moiety. Compound 4g [3-(1,2-dihydro-6-(3-nitrophenyl)-2-thioxopyrimidin-4-yl)-1-methylquinolin-2(1H)-one] also demonstrated considerable AChE inhibition. Kinetic studies provided further insights, compound 4e showed a competitive inhibition pattern at both low and high inhibitor concentrations. Compound 4g displayed mixed-type inhibition, suggesting its ability to interact with both the catalytic anionic site (CAS) and the peripheral anionic site (PAS) of AChE. Molecular docking of compounds 4a-j supported the experimental findings, with docking scores ranging from moderate to good compared to the reference drug. Notably, compound 4g had the best docking score of -10.134, forming a key hydrogen bond with PHE295, correlating well with its strong AChE inhibition. Further molecular dynamics simulations of compound 4g within the AChE binding site confirmed its stable interactions and potential binding mode. Based on these findings, compound 4g emerges as a promising lead molecule for the development of novel anti-Alzheimer agents. Finally, drug-likeness properties of all synthesized compounds were evaluated, supporting their potential for further development.



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Session 5. Natural Products and Biopharmaceuticals

sciforum-152050: *In silico* prediction of the antagonistic activity of natural compounds on neuropeptide S receptor 1 in endometriosis

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Endometriosis, an emerging disease affecting approximately 25% of women of reproductive age, presents a complex clinical profile, primarily characterized by dysmenorrhea, bleeding, infertility, and chronic inflammation. Currently, the Neuropeptide S Receptor 1 (NPSR1) is the genetically validated therapeutic target for the treatment of endometriosis, as its blockade prevents the binding of its endogenous ligand (neuropeptide S), thereby inactivating intracellular metabolic pathways related to pain and inflammation mechanisms. Natural compounds have served as structural models for the development of new drugs. Based on the mechanism of its selective antagonist SHA-68R, the structural fragment "CNC(=O)N" was searched across various natural product databases, selecting 54 molecules. These were subsequently analyzed through 2D-QSAR of their molecular descriptors to predict antagonist activity (pK_B). Their physicochemical and pharmacokinetic properties were evaluated *in silico* using SwissADME and Deep-pkCSM, along with their interactions with the NPSR1 receptor (retrieved in PDB format from the GPCR database using the code npsr1_human). To predict binding affinity energy (ΔG°), VINA 1.1.2 was used, and the molecules with the best parameters were visualized using the 2D tool in Discovery Studio. Rotihabin B exhibited optimal binding affinity (-8.7 kcal/mol), likely due to the formation of multiple hydrogen bonds. Its physicochemical profile exceeds Lipinski's parameters, with a suitable pharmacokinetic profile compared to the antagonist SHA-68R. This research proposes this metabolite as a starting molecule for the design of more potent compounds for the treatment of this disease, thereby improving the quality of life for those affected.



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sciforum-151238: *In vitro* activity of *Andrographis paniculata* (Burm.f.) Wall.ex Nees leaves ethanolic extract inhibits host cell invasion and intracellular replication of *Toxoplasma gondii* via modulation of protein kinase G (PKG).

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Introduction: Toxoplasmosis remains globally relevant because of its consequences on pregnancy outcomes, mental disorders, and opportunistic tendencies in immunocompromised individuals. Current medications have severe side effects on the host, low efficacy against the parasites, and potential development of resistance. This emphasizes the need to discover better and safer drugs to treat toxoplasmosis. This study evaluated the *in vitro* effects of ethanolic leaf extracts of *Andrographis paniculata* (EEAP) on protein kinase G (PKG) involved in cell invasion by *T. gondii*. **Methods:** EEAP was obtained through the maceration of dried leaf powder and then subjected to qualitative and quantitative screening of phytochemicals. Vero cells infected with the RH strain of *T. gondii* were used to evaluate the cytotoxicity and antiparasitic potential of EEAP, andrographolide, and clindamycin using the MTT assay. Microscopy was used to determine the cell invasion and intracellular replication of tachyzoites in the treated infected Vero cells at 24 h using 4 h post-infection treatment models. Gene expression profiling of *TgPKG* was performed using RT-qPCR. The expression of microneme proteins was determined using immunoblotting. **Results:** EEAP was found to contain more terpenoids. EEAP, andrographolide, and clindamycin were safe for host cells. EEAP and andrographolide exhibited good anti-parasitic activities against *T. gondii*. Microscopic assessment revealed a low infection index and intracellular replication by EEAP and andrographolide. RT-qPCR revealed a significant ($P=0.002$) downregulation of the *TgPKG* gene by 0.114-fold (88.6% decrease) and 0.068-fold (93.2% decrease), respectively, compared with the control. The expression of *TgMIC1* (0.442-fold, 55.8% decrease) and *TgMIC2* (0.385-fold, 61.5% decrease) proteins significantly ($P=0.0001$) decreased compared to the control. **Conclusion:** This study showed that EEAP and andrographolide are promising drug candidates effective against *T. gondii*, safe for the host cells, and can be used for the development of a potent anti-Toxoplasma drug to target the *TgPKG* gene involved in cell invasion to prevent disease progression.



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***sciforum-152243: Manilkara zapota* L. P. Royen Mitigates Chronic Asthma in Rats by Targeting the IL-1 β Pathway: Role of β -sitosterol as an Effective Component**

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Asthma, a chronic inflammatory disorder of the airways, presents a significant global health burden. The search for effective therapeutic interventions, especially from natural sources, remains imperative. Our study investigates the therapeutic potential of *Manilkara zapota* L. P. Royen (Sapodilla) in alleviating chronic asthma in rats. It elucidates its mechanism of action, focusing on the interleukin-1 beta (IL-1 β) pathway while identifying β -sitosterol as a crucial bioactive compound.

Using a rat model of chronic asthma induced by ovalbumin sensitization and challenge, we demonstrate that *M. zapota* administration effectively attenuates airway inflammation and hyperresponsiveness. Histopathological analysis reveals reduced inflammatory cell infiltration and mucus hypersecretion in the lung tissues of treated rats. Mechanistically, our findings indicate that *M. zapota* treatment significantly decreased IL-1 β , a key mediator of airway inflammation. Additionally, our investigation identifies β -sitosterol, a phytosterol abundant in *M. zapota*, as a major bioactive constituent responsible for its therapeutic effects in asthma.

This study sheds light on the therapeutic potential of *M. zapota* in managing chronic asthma by targeting the IL-1 β pathway, offering insights into the underlying mechanisms of action. Furthermore, identifying β -sitosterol as a key component underscores the importance of natural products in drug discovery and development for respiratory disorders. These findings warrant further exploration and potential clinical translation of *M. zapota* based therapies for asthma management.



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sciforum-149462: *Parmeliaceae* Lichens as Sources of Antioxidant Metabolites with Pharmacological Value

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Lichens are a valuable source of secondary metabolites with high antioxidant and therapeutic potential. This study evaluated the antioxidant activity of methanolic extracts from three species of the *Parmeliaceae* family—*Parmelia discordans*, *Parmelia saxatilis*, and *Xanthoparmelia tinctoria*—. Antioxidant activity was determined using ORAC, FRAP and DPPH assays. The phenolic compound content was also evaluated, using the Folin-Ciocalteu assay.

Parmelia discordans showed the highest ORAC value (24.94 $\mu\text{mol TE/mg}$) and a considerable phenolic content (106.49 $\mu\text{g AG/mg}$), indicating strong radical scavenging capacity associated with phenolic metabolites. *Parmelia saxatilis* exhibited a balanced profile, with high ORAC activity (19.03 $\mu\text{mol TE/mg}$), relevant reducing power (FRAP = 1.029 Eq Fe^{2+}/g), and strong DPPH activity ($\text{IC}_{50} = 814.42 \mu\text{g/mL}$), together with high phenolic content (97.86 $\mu\text{g AG/mg}$). *Xanthoparmelia tinctoria* displayed the highest reducing capacity (FRAP = 2.295 Eq Fe^{2+}/g) and the most potent DPPH activity ($\text{IC}_{50} = 642.93 \mu\text{g/mL}$), despite its low phenolic content (20.13 $\mu\text{g AG/mg}$). This finding suggests that non-phenolic compounds may play a central role in its antioxidant potential.

Additionally, methanolic extracts were tested on human neuroblastoma SH-SY5Y cells to assess their effects on cell viability, resistance to oxidative stress, and intracellular generation of reactive oxygen species (ROS). The combined biochemical and cellular data highlight complementary antioxidant strategies: phenolic-driven activity in *P. discordans*, a robust and balanced profile in *P. saxatilis*, and non-phenolic but highly effective mechanisms in *X. tinctoria*.

These findings support lichens as promising candidates for further phytochemical and pharmacological research focused on natural antioxidant agents. Nevertheless, it is necessary to continue researching.



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sciforum-151296: Antioxidant Activity of Astaxanthin Extracts Obtained from Shrimp Shells

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Introduction: Astaxanthin is a widely studied carotenoid due to its health-promoting properties. It has been reported to possess antibacterial, antimicrobial, anti-inflammatory, anticancer, and antioxidant properties, making it a valuable compound in the development of cosmetics, nutraceuticals and pharmaceuticals. In recent years, marine waste, such as shrimp shells, has been investigated as a source of astaxanthin. This study aimed to investigate the antioxidant capacity of astaxanthin extracts obtained from shrimp shells. **Methods:** Shrimp shells were collected, cleaned, dried, and subjected to ultrasound-assisted extraction to obtain astaxanthin-rich extracts. The antioxidant capacity of the extracts was evaluated using widely established radical scavenging assays, including DPPH and ABTS. The results were expressed as EC50 values and compared with ascorbic acid as a standard antioxidant.

Results: The shrimp shell extract showed potent antioxidant activity at low concentrations. In the DPPH assay, it achieved over 90% radical scavenging at 1.0 µg/mL, with an EC50 of 0.37 µg/mL. By comparison, ascorbic acid was far less potent (EC50 = 6.89 µg/mL) and reached only 60% scavenging at its highest tested concentration (7.5 µg/mL). Similar results were observed in the ABTS assay, where the shrimp shell extract achieved nearly complete inhibition at concentrations below 1 µg/mL (EC50 = 0.13 µg/mL), outperforming the positive control (EC50 = 1.74 µg/mL).

Conclusions: These findings demonstrate that astaxanthin extracts from shrimp shells exhibit strong antioxidant activity, making it highly suitable as a natural bioactive ingredient. Such extracts have clear potential for incorporation into nutraceuticals, functional foods, and cosmetic formulations, providing a sustainable route to natural antioxidant enrichment in commercial products.



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sciforum-151602: *Artemisia herba alba* for Arthritis: A Safer, Natural Alternative to Indomethacin

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The clinical management of rheumatoid arthritis continues to demand the development of effective and safer alternatives to traditional non-steroidal anti-inflammatory drugs (NSAIDs), which are often limited by significant adverse effects. This research investigated the therapeutic potential of an extract derived from *Artemisia herba alba* using a well-established rat model of Complete Freund's Adjuvant (CFA)-induced arthritis. Over a 15-day treatment period, animal groups received oral administrations of the plant extract at one of two doses (250 or 500 mg/kg), the standard drug indomethacin (3 mg/kg), or a saline control. The results demonstrated that the higher dose of *Artemisia herba alba* (500 mg/kg) produced a highly significant reduction in paw swelling, decreasing the measurement from 5.68 ± 0.06 mm to 4.65 ± 0.02 mm ($p < 0.001$). Furthermore, it effectively alleviated pain hypersensitivity, reversing response rates from $70 \pm 6.1\%$ to $10 \pm 3.2\%$ ($p < 0.001$). On a biochemical level, the treatment enhanced the body's innate antioxidant defenses while successfully reducing markers of lipid peroxidation. Most notably, in stark contrast to indomethacin, which induced clear hepatotoxicity and a pronounced oxidative stress state (MDA: 4.25 ± 0.41 $\mu\text{mol/L}$), the plant extract demonstrated a protective effect on liver and kidney function. Histological analysis of joint tissue corroborated these findings, showing markedly reduced inflammation and cellular infiltration. Collectively, these findings strongly advocate for *Artemisia herba alba* extract as a potent, dual-action, and notably safer natural therapeutic candidate for the treatment of inflammatory arthritic conditions.



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sciforum-145662: Effect of microencapsulation and freeze-drying on the functional properties of *Spondia mombin* stem extract used in ethno-medical management of benign prostrate hyperplasia

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Introduction: Different techniques have been used to improve the stability and bioavailability of biomaterials. This study aims to modify the crude stem extract of *Spondia mombin* used in ethno-medical management of benign prostrate hyperplasia (BPH).

Methods: *Spondia mombin* stem extract was modified by microencapsulation and freeze drying, and characterised using scanning electron microscopy (SEM), energy dispersive X-ray (EDX), and Fourier transform infrared spectroscopy (FTIR) analysis. The extracts were evaluated for physicochemical properties using micromeritic determination and dissolution studies, and for in vivo pharmacological properties using prostate-specific antigen (PSA), serum testosterone, and prostate index (PI) analysis on male Wister rats.

Results: SEM analysis showed a larger particle size of 50–80 µm for microencapsulated extract compared to >50 µm of crude extract. FT-IR and EDX analysis revealed relatively unchanged spectrum and additional molecules respectively in the modified extract compared to the crude extract. These results are suggestive of chemical compatibility and physical agglomeration in the interaction of the crude extract with microencapsulation excipients. Dissolution studies revealed steady release of extract from the microencapsulated form over 60 minutes, and > 9.76 times increase in peak release compared to release from the crude extract. The micromeritic studies showed improved flow properties for the microencapsulated extract with angle of repose 27.9°, Hausner's ratio 1.06, and compressibility index 6.06 %. The microencapsulated extract showed peak reduction in PSA at 100 mg / kg, compared to peak reduction of PSA of crude extract at 400 mg / kg. Serum testosterone levels decreased significantly in the microencapsulated extract.

Conclusion: Microencapsulation improved the flow and dissolution properties of *Spondia mombin* extract, and retained its pharmacological activities. There is a need to conduct human clinical trials to further explore the potentials of this microencapsulated



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sciforum-152065: Essential oils and the post COVID-19 mental health crisis: literature analysis based on VOSviewer

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Introduction: There is a global concern about COVID-19 long-term impact on multiple domains of life. The WHO has raised concerns regarding the pandemic's psycho-social and mental health consequences. Many recent articles explored the efficacy of using aromatic plants essential oils (EOs) as promising candidates for management of different mental health issues. **Objectives and Methods:** A co-occurrence analysis of the available literature from Scopus, Web of science, and PubMed databases was conducted using network and overlay visualization created via VOSviewer software to examine the role of EOs in alleviating mental health crisis in the post-COVID-19 era. **Results:** The United States and China emerged as the leading contributors to the literature, followed by India and Iran. The authors affiliated with Tehran University of Medical Sciences produced the highest volume of research in this field. The analysis showed a progressive growth in publication volume, rising from 8 documents in 2015 to 27 in 2025, with a significant spike occurring in 2019 and 2020 coinciding with the COVID-19 pandemic. Results revealed that terms such as mental health, stress, depression, insomnia, and anxiety are common search terms in literature and exhibit strong associations with aromatherapy and COVID pandemic. The most frequently used EOs in the context of mental health improvement are lavender (Occurrence 8, TLS 92), bergamot (occurrence 5, TLS 53), peppermint, chamomile and rosemary. EOs exert antidepressant, anxiolytic, and anti-stress effects, which contribute to their therapeutic potential in enhancing psychological well-being. **Conclusions:** This analysis simplifies the data, enabling researchers to trace past work and outline future directions.



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sciforum-151641: Exploring Terrestrial and Marine Fungi for New Anticancer Agents from Saudi Arabia's Ecosystem

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Background

Cancer is a major global health concern, with 24,485 new cases and 10,518 deaths in Saudi Arabia in 2020. Fungi produce bioactive compounds with anticancer and antimicrobial potential. This study investigates fungal metabolites from Saudi soil to identify novel therapeutic agents, addressing gaps found in our previous systematic review.

Methods

Seventeen fungal strains were isolated from soil samples collected at five locations in Riyadh and Hail. Samples were plated on Potato Dextrose Agar, incubated to obtain pure cultures, and extracted using a yeast malt extract medium. The cytotoxic effects of the extracts were assessed via an MTT assay against MDA-MB-231 (breast cancer) and HCT-116 (colorectal cancer) cell lines. Additionally, antimicrobial activity was evaluated against Methicillin-resistant *Staphylococcus aureus* (MRSA), *Candida* spp., and *Escherichia coli* at concentrations ranging from 0.3 mg/mL to 5 mg/mL.

Results

The fungal extracts exhibited notable cytotoxicity against MDA-MB-231 cells, with IC₅₀ values ranging from 28.55 to 83.35 µg/mL. Additionally, six extracts tested against HCT-116 cells demonstrated potent activity, with IC₅₀ values between 22.25 and 71.63 µg/mL. In antimicrobial testing, initial results showed no significant activity against MRSA, *Candida* spp., or *E. coli*, which may be due to the low concentrations used. Further testing at higher concentrations is planned to explore potential antimicrobial effects.

Conclusion

This study highlights Saudi soil fungi as a promising source of anticancer agents. Although antimicrobial activity was insignificant at low concentrations, further testing is needed. Exploring regional biodiversity may lead to new drug discoveries, and future research will focus on identifying active compounds and their mechanisms of action.



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sciforum-152071: Mansonone G as a Natural Neuroprotective Compound in a Zebrafish Model of Alzheimer's Disease

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder with a significant global impact, and current treatments provide limited benefits with frequent side effects. This has prompted growing interest in natural compounds with neuroprotective potential. Mansonone G, a natural compound isolated from *Mansonia gagei*, is recognized for its antioxidant and anti-inflammatory properties. The present study evaluated the effects of Mansonone G on memory using zebrafish (*Danio rerio*) as a preclinical AD model. Cognitive deficits were induced by exposing zebrafish to okadaic acid (OKA, 10 nM) for 4 days. Animals (n = 10 per group) were allocated to six groups: control (DMSO), galantamine (1 mg/L) as a positive control, OKA with DMSO (amnesia model), and OKA with Mansonone G at doses of 1, 3, or 6 µg/L. Mansonone G was administered every three days for 7 days with water renewal. Cognitive performance was assessed by the Y-maze test for spatial memory and locomotor activity and the Novel Object Recognition (NOR) test for recognition memory. OKA exposure significantly impaired memory and recognition (p 0.0001), while galantamine restored cognitive performance. Treatment with Mansonone G at 3 and 6 µg/L significantly improved spatial memory and object recognition, with p 0.001 for 3 µg/L and p 0.00001 for 6 µg/L, and enhanced locomotor activity. The 1 µg/L dose had minimal impact. Mansonone G demonstrated neuroprotective effects by increasing exploratory behavior, improving recognition memory, and restoring cholinergic function in OKA-treated zebrafish, supporting its development as a natural therapeutic candidate for AD.



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sciforum-150469: NMR and DFT Study of Chondroitin Sulphate

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Chondroitin sulphate is a sulphated glycosaminoglycan (GAG), abundantly present in connective tissues, particularly articular cartilage. There, it plays a critical role in maintaining structural integrity and elasticity. As a key component of the extracellular matrix, it is involved in various biological processes, including cellular signalling pathways, tissue hydration, and matrix organisation [1,2]. Furthermore, the therapeutic potential of chondroitin sulphate as an agent in joint-related disorders such as osteoarthritis has been studied due to its anti-inflammatory and cartilage-protective properties [3,4]. The therapeutic potential of chondroitin sulphate lies in its ability to reduce cartilage catabolism by inhibiting extracellular matrix degradation [5].

The combination of NMR spectroscopy and density functional theory (DFT) provides valuable insights into the structure, dynamics, and solubility of glycosaminoglycans [6]. In this study, DFT calculations were performed using the MN15/6-311++G(2d,2p)//SMD approach to determine the 3D structures of chondroitin 6-sulphate and chondroitin 4-sulphate tetrasaccharides. Computed proton–proton and proton–carbon coupling constants revealed that the one-bond proton–carbon coupling constants ($^1J_{C-H}$) depend strongly on the substitution position (C-6 vs. C-4). However, substitution also affects the $^1J_{C-H}$ and $^3J_{C-H}$ magnitudes in the neighbouring atoms. The $^1J_{C-H}$ values were consistent with the experimental NMR values. The $^3J_{C-H}$ values also revealed differences in the glycosidic linkages in chondroitin tetrasaccharides. These findings demonstrate that the position of sulphate groups on the chondroitin backbone significantly affects electronic distribution, geometry, and $^nJ_{C-H}$ magnitudes, thereby highlighting the role of hydrogen bonding and ionic interactions in the 3D structure of chondroitin tetrasaccharides.

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sciforum-151426: Preliminary Studies on Plant-derived Natural Indicators for Pharmaceutical Applications

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Indicators used in titration are generally chemical dyes of synthetic origin that provide distinct color transitions of pH. Nature has abundant source of plants that need to be identified for their indicator property there by promoting SDG 12 (Responsible Consumption and Production) and SDG 15 (Life on Land) goal. The present study focuses on the applicability of vegetables' and fruits' extracts as natural indicators. A comparative study of red cabbage (*Brassica oleracea*), dragon fruit (*Selenicereus undatus*), pomegranate (*Punica granatum*), beetroot (*Beta vulgaris*) and turmeric (*Curcuma longa*) extracts with synthetic indicator viz. phenolphthalein was carried out to evaluate their potential as acid-base indicator. The findings revealed that all plant extracts tested were effective as acid-base indicators in strong acid-strong base titrations. Additionally, red cabbage (*Brassica oleracea*) and dragon fruit (*Selenicereus undatus*) demonstrated indicator activity even in strong acid-weak base titrations. The study detected the presence of anthocyanins in all plant extracts which were analysed by determining their $\lambda_{\max}$ by UV spectrophotometry and R_f by Thin Layer Chromatography. The choice of such natural indicators can be explained by their wide occurrence, non-toxicity, simple methods of extraction, and low cost, which makes these indicators a sustainable alternative to synthetic ones in the context of pharmaceutical use.



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sciforum-152240: The Combination Between a Standardized Extract of Brazilian Red Propolis with Praziquantel Against *Schistosoma mansoni* *In Vitro*

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Introduction: Although praziquantel (PZQ) is being used for treatment of schistosomiasis, the description of regions which harbor *Schistosoma* strains that are less sensitive to PZQ underscores the need to identify new alternative to treat this disease. Combination therapy has become a promising strategy for several complex diseases which it can increase therapeutic efficacy, reduce toxicity and overcome drug resistance compared with single-drug administrations. Thus, as part of our contribution to developing the strategies for treatment against schistosomiasis, we evaluate the combination of PZQ with a standardized extract of Brazilian red propolis (SEBRP), a resinous bee product that presents several biological effects, on *S. mansoni* adult worms *in vitro*. **Methods:** Adult worms were obtained by perfusion and cultivated in RPMI 1640 medium. Dose– response relationships were established following exposure of adult *S. mansoni* to SEBRP, PZQ and fixed concentration combinations of SEBRP/PZQ *in vitro* after 24, 48 and 72 hours. **Results:** PZQ and SEBRP shows an effective concentration of 50% of 0.045µg/mL and 6.14µg/mL at 72 hours, respectively. PZQ/SEBRP combination showed synergistic effects against adult worms after 72 hours of incubation, with combination index (CI) values lower than 1.0 when adult *S. mansoni* were simultaneously incubated with both drugs *in vitro*. **Conclusion:** Based on these data, it was possible to observe that SEBRP plays an important schistosomicidal action in adult worms. In addition, combination of PZQ/SEBRP may be a promising strategy to treatment for schistosomiasis.



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sciforum-148274: Therapeutic Potential of *Mandragora autumnalis*: Inflammation Modulation and Antimicrobial Properties

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Inflammation is an essential immune defense mechanism that protects the body from infections and tissue injury; however, when dysregulated or persistent, it becomes a pathological driver of chronic diseases. It is an essential immune response; however, its chronic activation contributes to the development of several disorders, including arthritis, cardiovascular diseases, and certain types of cancer. Natural plant extracts, enriched with bioactive compounds, have long been employed in traditional medicine to alleviate inflammation by modulating immune pathways. *Mandragora autumnalis* (MAE), traditionally recognized for its anticancer, antioxidant, and antimicrobial properties, is rich in phenols, flavonoids, and alkaloids; however, its anti-inflammatory mechanisms remain poorly understood. This study investigated the effects of ethanolic MAE extract in lipopolysaccharide (LPS)-stimulated RAW 264.7 macrophages. Treatment with MAE significantly suppressed the expression of pro-inflammatory mediators, including cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS). Furthermore, MAE reduced macrophage migration and regulated critical inflammatory signaling pathways, notably NF- κ B, STAT-3, and MAPKs. Beyond its immunomodulatory activity, MAE exhibited broad-spectrum antimicrobial effects against diverse pathogenic bacterial and fungal strains. Collectively, these findings suggest that MAE possesses dual anti-inflammatory and antimicrobial properties, underscoring its potential as a natural therapeutic agent. Further studies are warranted to elucidate its molecular mechanisms and to explore its possible applications in the prevention and management of inflammation-associated disorders and infectious diseases.



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sciforum-144611: An insight into the antimalarial and antioxidant properties and pharmacognostic standards of the leaves of *Bambusa vulgaris* (Schrad). ex J.C.Wendl.

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Introduction: Malaria remains a significant public health concern in Ghana, underscoring the need to explore the antimalarial efficacy of medicinal plants, such as *Bambusa vulgaris* (bamboo), traditionally used for its management. This study investigates the in vivo antimalarial efficacy of aqueous (BVA) and hydroethanolic (BVE) leaf extracts of *B. vulgaris* against *Plasmodium berghei*-infected mice, alongside their antioxidant activity and pharmacognostic standards.

Method: Acute toxicity was assessed following OECD guidelines. Antimalarial activity was evaluated using Peter's four-day suppressive and Rane's curative tests. Antioxidant properties were investigated using the DPPH assay. Pharmacognostic standards were established following standard procedures.

Results: The LD₅₀ of the extracts was > 2000 mg/kg. In the four-day suppressive test, BVE exhibited parasitaemia suppression and an ED₅₀ of 90.68 ± 1.53% at 400 mg/kg and 177.83 ± 16.36 mg/kg, respectively. BVA, similarly, provided a suppression and an ED₅₀ of 84.98 ± 1.62% and 281.84 ± 22.31 mg/kg. In the curative test, BVA achieved a % suppression of 63.15 ± 1.53 at 400 mg/kg and an ED₅₀ of 234.42 ± 10.28 mg/kg. Both extracts prolonged survival and increased body weight of mice, with BVA reversing hypothermia and anaemia. Antioxidant assays revealed BVE's stronger DPPH scavenging activity, with an IC₅₀ of 851.3 µg/mL, compared to BVA, which had an IC₅₀ of 1552 µg/mL, attributed to higher flavonoid (4.71 ± 0.039 mg quercetin/g) and phenolic (58.99 ± 0.039 mg GAE/g) contents. Pharmacognostic studies established macro-morphological, microscopic, physicochemical, chromatographic, and spectroscopic standards.

Conclusion: The study validates the traditional antimalarial use of *B. vulgaris* leaves and provides standard benchmarks for its quality control.



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sciforum-150510: Anti-Elastase and Anti-Tyrosinase Activities of *Cistus salviifolius* and *Cistus laurifolius* Leaf Extracts: Potential Natural Agents for Skin Regeneration and Depigmentation.

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Background: Skin aging and pigmentation disorders are influenced by both intrinsic factors (genetics, metabolism, hormones) and extrinsic factors (ultraviolet radiation, pollution, chemicals). These factors contribute to progressive structural and functional alterations of the skin, clinically manifested as wrinkles, loss of elasticity, and hyperpigmentation. Among the key enzymes implicated in these processes are elastase and tyrosinase. In response to the growing demand for safer and more sustainable cosmetic ingredients, plant-derived extracts have attracted considerable interest as sources of natural anti-aging and depigmenting agents.

Methods: The present study investigated *in vitro* the inhibitory activities of hydroethanolic leaf extracts of *Cistus salviifolius* (CSLE) and *Cistus laurifolius* (CLLE) using spectrophotometric enzyme assays. Enzymatic inhibition was assessed using N-succinyl-Ala-Ala-Ala-p-nitroanilide as substrate for elastase and L-DOPA for tyrosinase, with elastatinal and kojic acid employed as reference inhibitors, respectively.

Results: CSLE exhibited notable anti-elastase activity with an IC_{50} value of 43.0 $\mu\text{g/mL}$, significantly lower than that of CLL (IC_{50} = 218.2 $\mu\text{g/mL}$), while the positive control elastatinal displayed an IC_{50} of 0.5 $\mu\text{g/mL}$. Regarding tyrosinase inhibition, CSLE (IC_{50} = 28.7 $\mu\text{g/mL}$) and CLL (IC_{50} = 30.2 $\mu\text{g/mL}$) demonstrated comparable activities, both slightly exceeding the efficacy of kojic acid (IC_{50} = 31.1 $\mu\text{g/mL}$).

Conclusion: These findings highlight the potential of CSLE and CLL extracts, particularly CSLE, as valuable natural sources of elastase and tyrosinase inhibitors, thereby supporting their prospective application in the formulation of cosmeceutical products.



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sciforum-152015: Anti-Inflammatory Potential of *Albizia lebbbeck*: *In Vivo* Evidence and Scientometric Analysis

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A

Introduction: *Albizia lebbbeck* is widely used in traditional Indian folk medicine to treat several inflammatory pathologies, such as asthma and arthritis. **Objectives and Methods:** The present study aims to scientifically investigate *A. lebbbeck* claimed anti-inflammatory effect using the rat paw edema model. Additionally, a co-occurrence analysis of the available literature from Scopus, Dimensions, PubMed, and lens.com databases was conducted using network and overlay visualization (VOS viewer) to present a detailed bibliometric and scientometric analysis concerning its potent anti-inflammatory potential and to explore the existing knowledge gaps and the required future research directions. **Results:** The *in vivo* results revealed that *A. lebbbeck* (100 mg/kg) reduced significantly the edema volume by 37.27% and 31.43% compared to the carrageenan/diclofenac group (35.90% and 51.79%) after 1 and 3 hrs of carrageenan injection, respectively. This observed anti-inflammatory potential represents 103.8% (1 hr) and 60.7% (3 hrs) of diclofenac sodium efficacy. Luteolin and kaempferol were detected in the extract under investigation and they contribute to the proven anti-inflammatory potential. Networking analysis revealed that the *Journal of Ethnopharmacology* is the most productive publisher concerning *A. lebbbeck* anti-inflammatory potential. The publication volume showed steady growth, increasing from 65 documents in 2015 to 182 in 2025, with notable peaks observed in 2021 and 2024. Over half of these publications were original research articles, with *Biomedical and clinical sciences* being the leading subject area. Terms such as terpenoids, flavonoids, saponins, and tannins are common search terms exhibited strong associations with *A. lebbbeck* anti-inflammatory properties. **Conclusions:** This study scientifically supports the traditional anti-inflammatory use of *A. lebbbeck* and recommends further mechanistic studies on its isolated phytochemicals to link this potent activity with the bioactive compounds. Detailed clinical studies are urgently needed to confirm its efficacy and therapeutic potential.



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sciforum-146389: Anti-inflammatory Potential of Selected Indian Medicinal Plants

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Arthritis, a progressive inflammatory disorder, significantly impacts joint health and quality of life. Despite advancements in medical treatments, there remains a growing interest in traditional medicine systems for their holistic approaches and reduced risk of side effects. This study evaluates the anti-inflammatory and therapeutic potential of an Unani formulation comprising *Anthemis nobilis* Linn, *Eucalyptus globulus*, *Ferula assa-foetida*, *Hyoscyamus niger*, *Styrax benzoin*, and *Sesamum indicum*. Phytochemical screening revealed the presence of key bioactive compounds, including total phenolic content (TPC) and total flavonoid content (TFC), which contribute to their therapeutic properties. Antioxidant assays, such as DPPH, ABTS, FRAP, and NO, were performed using aqueous plant extracts to evaluate their free radical scavenging activity. Among the extracts, *Ferula assa-foetida* exhibited the highest antioxidant activity in both DPPH and ABTS assays, while *Eucalyptus globulus* showed the highest activity in the FRAP assay. For NO scavenging activity, *Sesamum indicum* demonstrated the strongest antioxidant potential. Acute toxicity testing was conducted on rats to evaluate the safety of these plants. Results indicated no toxic effects on the skin or other observed parameters, confirming their safety. Cytokine profiling studies revealed significant downregulation of key pro-inflammatory markers, including TNF- α and IL-6, highlighting the formulation's potential to modulate inflammatory pathways effectively. These findings suggest that the selected plants can mitigate oxidative stress, reduce inflammation, and support joint health, providing a natural and effective alternative for arthritis management. The study underscores the potential of these medicinal plants as accessible, sustainable therapeutic options that integrate traditional practices with scientific validation.



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sciforum-150197: Antibacterial potential of *Emblica officinalis* endophytes against multidrug-resistant avian pathogenic *Escherichia coli* (APEC)

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Colibacillosis remains a major threat to the poultry industry of Pakistan, leading to significant economic losses. The disease is caused by avian pathogenic *Escherichia coli* (APEC), which induces multiple complications leading to prolonged and irrational antibiotic use. This is resulting in the emergence of multidrug-resistant APEC strains, highlighting the urgent need for alternative control strategies. Medicinal plants and their endophytic microbiota represent promising sources of bioactive compounds with antimicrobial potential, as they have co-evolved with their host plants and often mimic or enhance host defense mechanisms. In this study, bacterial endophytes were isolated from *Emblica officinalis* (Amla), a medicinal plant widely used in traditional medicine, and their extracts were tested for antibacterial activity against pre-confirmed APEC strains using the agar well diffusion method. To provide a comparative analysis, fruit extracts of *E. officinalis* were also evaluated for antibacterial activity under the same conditions. The endophytic extracts exhibited significantly stronger antibacterial activity (28 mm inhibition zone) than the fruit extracts (16 mm inhibition zone), indicating the superior potency of endophyte-derived metabolites. Partial purification via thin layer chromatography (TLC) confirmed distinct active components responsible for this activity. These findings suggest *E. officinalis* endophytes as valuable candidates for alternative, sustainable approaches against antibiotic-resistant poultry pathogens.



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sciforum-152360: Antibacterial, antiobesity, and toxicity effects of cherry stem ethanolic extract

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Due to their increasing prevalence, obesity and infectious diseases represent major public health problems, which is why effective therapeutic alternatives need to be found. There is considerable interest in the potential health benefits of cherry stems, a by-product of the agri-food industry. In this work, we studied the impact of the ethanolic extract of cherry stems on the inflammation and oxidative stress associated with obesity, as well as its antibacterial effect. In addition, acute oral toxicity was assessed in female BALB/c mice. Furthermore, the quantity of bioactive substances was estimated in the cherry stems extract. To do this, a phytochemical analysis was carried out, then the biological activities related to obesity reduction were examined *in vitro* and *in vivo*. The effect of the extract on several pathogens was also assessed, as well as its synergy with antibiotics. The *in vitro* studies have shown significant amounts of vitamin C and phenolic compounds (3.93 mg ASE/g and 215.52 ± 2.46 mg GAE/g extract, respectively). At a concentration of 01 mg/ml, the extract showed a significant anti-inflammatory (67.11%), antioxidant (60.17 and 64.23%) and anti-obesity (28.29 and 76.66%) properties. The acute oral toxicity of crude ethanolic cherry stem extract, even at high doses, revealed no observable toxicity. The data indicate that cherry extracts exhibit significant antimicrobial activity, with growth inhibition levels ranging from 10 to 98.50%. This is mainly attributed to their bioactive composition. When this extract is combined with antibiotics, they enhance the inhibition of bacterial proliferation, showing an encouraging synergistic effect. In addition, this plant has demonstrated bactericidal action (66.66 - 77.77%) against various strains of pathogenic bacteria. All these factors suggest that cherry stems could be a natural alternative for combating bacterial infections and obesity and their related disorders.



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sciforum-150793: Antimycobacterial and Anti-Inflammatory Potential of the Antarctic Alga *Desmarestia anceps*: Identification of Potential Leads

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Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (Mtb), remains the leading cause of infectious mortality worldwide, and the emergence of drug-resistant strains has intensified the search for new therapeutic agents. Marine macroalgae from underexplored ecosystems such as Antarctica represent promising sources of bioactive metabolites. Here, we investigated the antimycobacterial and anti-inflammatory potential of *Desmarestia anceps*. Crude extracts from eight sites across the Antarctic Peninsula were screened, among which the extract from Penguin Island exhibited the strongest effect against Mtb H37Rv ($MIC_{50} = 6.6 \mu\text{g/mL}$) and concomitant reduction of nitric oxide ($IC_{50} = 4.2 \pm 1.1 \mu\text{g/mL}$) and TNF- α production ($IC_{50} = 21.4 \pm 1.1 \mu\text{g/mL}$). Bioassay-guided fractionation identified DAF2 as the most promising, displaying potent antimycobacterial effects ($MIC_{50} = 16.9 \mu\text{g/mL}$ against H37Rv), no cytotoxicity in murine macrophages ($CC_{50} > 100 \mu\text{g/mL}$), and suppression of NO levels in LPS-stimulated macrophages, thus suggesting a dual role in infection control and inflammation modulation. High-speed counter-current chromatography (HSCCC) of DAF2 revealed sterols, fatty acids and diterpenoids as major constituents, among which saringosterol—previously shown to have potent antimycobacterial activity—and fucosterol were prominent. Fucosterol, isolated and tested individually, exhibited remarkable activity against Mtb H37Rv ($MIC_{50} = 0.37 \pm 0.09 \mu\text{g/mL}$) and the hypervirulent strain M299 ($MIC_{50} = 3.05 \pm 1.11 \mu\text{g/mL}$), with a selectivity index above 10 based on macrophage cytotoxicity ($CC_{50} = 51.45 \mu\text{g/mL}$). Altogether, these findings highlight *D. anceps* as a promising source of natural products with combined antimycobacterial and anti-inflammatory activities, positioning fucosterol as a promising lead for TB drug discovery.



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sciforum-150985: Assessment of Hepato-Protective Potential of a Sinapic Acid on Animal Model of Alcohol Induced Hepatotoxicity

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Background:

Alcoholic liver disease (ALD) remains one of the major causes of liver-related morbidity and mortality worldwide. Oxidative stress and inflammation are key mechanisms driving hepatic injury. Sinapic acid (SA), a naturally occurring phenolic compound abundant in cereals, oilseeds, and vegetables, is recognized for its antioxidant and anti-inflammatory properties and has been identified in several traditional medicinal formulations.

Methods:

The present study evaluated the hepatoprotective efficacy of SA in Wistar albino rats exposed to ethanol-induced hepatotoxicity. Liver injury was induced by oral administration of ethanol (40%) for 21 days. SA was administered at doses of 40, 80, and 100 mg/kg p.o., and its protective effects were assessed through biochemical markers (SGOT, SGPT, ALP, total cholesterol, triglycerides, HDL), antioxidant parameters (GSH, MDA, CAT, SOD), proinflammatory cytokines (TNF- α , IL-6), and histopathological examination.

Results:

Ethanol exposure markedly increased ALT (154.2 ± 6.3 IU/L), AST (178.5 ± 8.1 IU/L), and ALP (326.4 ± 10.2 IU/L) compared with normal controls (48.3 ± 3.1 , 72.6 ± 4.8 , and 162.7 ± 7.5 IU/L; $p < 0.001$). SA at 80 and 100 mg/kg significantly reduced these levels, with ALT at 82.4 ± 5.2 and 76.8 ± 4.9 IU/L and AST at 102.3 ± 6.1 and 96.7 ± 5.4 IU/L. GSH levels increased from 18.3 ± 1.2 to 32.5 ± 1.8 μ mol/mg, while MDA decreased from 7.4 ± 0.5 to 3.2 ± 0.3 nmol/mg ($p < 0.001$). qRT-PCR revealed downregulation of TNF- α and IL-6 by 68% and 61%, respectively. Histological findings confirmed reduced necrosis and inflammation with near-normal hepatic architecture in treated groups.

Conclusion:

Sinapic acid exhibits strong hepatoprotective effects against alcohol-induced liver injury, likely through attenuation of oxidative stress and inflammatory pathways. These findings support its potential as a natural therapeutic candidate for managing ALD.



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sciforum-124801: Beta-catenin inhibitory phytocompound from Glycine max Seeds: In silico to in Vivo approach

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Ovarian cancer is lethal and 7th leading cause of deaths in females. Aberrant β -catenin in Wnt signaling works as a key player in cancer. Major functional components of soybean seeds possess multiple therapeutic activities. Results of UV-Vis. Spectroscopy and GC-MS analysis showed that ethanolic extract of *Glycine max* had highest concentration of 4',7-Dihydroxyisoflavone daidzein along with 9,12-Octadecadienoic acid(Z,Z)-, methyl ester, 12-Octadecenoic acid, methyl ester, 11-Octadecenoic acid, methyl ester, Linoleic acid ethyl ester, (E)-9-Octadecenoic acid ethyl ester and 4',7-Dihydroxyisoflavone Daidzein (retention time is 13. 797 min- 9.097 min). *In-silico* study showed that daidzein has maximum binding affinity with beta catenin, which may be inhibited. Results of *in vivo* study on normal cell lines showed that all extracts had varying effects on cell viability but n-hexane (20 μ g/mL) extract showed highest variation. DMBA induced adult healthy female *Sprague Dawley* rats (150-200 g) have been treated with paclitaxel, diadzin and polarity based extracts of *G.max* seeds (10 mg/Kg b.w) and results on CA 125 showed a steady increase but at a lower rate than the negative control group. Some extracts significantly reduced CA 125 levels, while a combination of Daidzein+Paclitaxel showed least CA 125 levels. Biochemical profile showed that the group treated with combination therapy showed protective effects with improved protein metabolism and lower urea, creatinine and bilirubin content while n-Hexane and ethanolic extracts exhibited moderate organ stress. Hematological parameters remained stable, with some groups showing improvements in RBC and hemoglobin levels. Daidzein and ethanolic extracts showed protective effects on ovary and liver while combination therapy reduced tumor growth and severe organ damage. Histological analysis showed that paclitaxel provided partial protection from tumor progression/ organ damage. Daidzein and ethanolic extracts showed protective effects. n-Hexane extract had variable effects, while other extracts showed moderate protective properties.



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sciforum-152312: BIOACTIVE PROPERTIES OF ETHANOL EXTRACTS *TARGETES PATULA* L. FLOWERS

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Introduction. Marigolds are characterized by a rich composition of biologically active substances, a complex effect on the body and low side effects. They are widely cultivated in Ukraine. However, activity of plants extracts depending on many factors, including the part of the plant, geographical source, extraction method, etc. So, we prepared extracts from marigold *Tagetes patula* L. flowers in 64% and 70% ethanol. The effects of the extracts on the morphological and functional properties of cells, antioxidant potential and antiviral activity were studied.

Methods. The influence of the extracts on viability of tumor cells (A549 – lung cancer and Hep-2 – laryngo carcinoma) were studied using fluorescence microscopy, MTT and trypan blue assays. The *in vitro* antioxidant activity of the extracts was measured by the free radical scavenging capacity according to the DPPH test. Antiviral activity was determined using yield reduction assay.

Results. Morphological changes of human tumor cell were detected, namely their rounding, granularity, increase in size, and swelling. The mitochondrial activity of the cells at the used concentrations of extracts was within 45 - 100%. However, a study of cell membrane permeability revealed inhibition of A549 and Hep-2 cells viability under the influence of extracts by 18-79% and 19-66%, respectively. In addition, analysis of the mitotic activity of tumor cells under the action of the extracts showed a significant decrease in their mitotic index. High antiradical activity and the ability of both extracts to absorb DPPH radical were shown. Also, a similar pronounced antiherpetic efficiency of both extracts was established, the decreasing of herpes simplex virus type 1 infectious titer was in the range of 1.7 - 4.7 log₁₀ TCID₅₀/ml.

Conclusions. These findings suggest, that extracts obtained from marigold *Tagetes patula* L. flowers may hold promise as a potential therapeutic agents.



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sciforum-149585: Bioactivity of *Pseudevernia furfuracea* Extracts: Antioxidant and Antibacterial Assessment

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Lichens represent a promising source of novel molecules with diverse biological activities. This study aims to evaluate the antioxidant and antibacterial properties of extracts from the lichen *Pseudevernia furfuracea* to assess its potential for valorization in the pharmaceutical and food industries. Following a preliminary morphological characterization of the thallus, extraction was performed via maceration using three solvents: methanol, ethyl acetate, and dichloromethane. Antioxidant activity was quantified through three distinct methods (DPPH, CAT, and FRAP assays), while antibacterial efficacy was tested against four ATCC-referenced bacterial strains (*Enterobacter cloacae* ATCC 13047; *Klebsiella pneumoniae* ATCC 700603; *Staphylococcus aureus* ATCC 25923 and *Staphylococcus aureus* ATCC 43300) using the agar diffusion technique. The results demonstrated significant antioxidant activity of the ethyl acetate extract (IC₅₀=71,72 µg/ml of DPPH assay and 66,66 mg EAA/g extract of cat assay), whereas the methanolic and dichloromethane extracts exhibited moderate activity. The results of the antibacterial activity assessment revealed that all tested strains exhibited susceptibility to the extracts. Notably, the ethyl acetate extract was found to be the most effective, demonstrating significantly greater efficacy than the other solvents used. The pronounced efficacy of the ethyl acetate extract is attributed to its richness in bioactive secondary metabolites, underscoring its potential for applications in medicinal and cosmetic formulations.



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sciforum-150758: Chemical Characterization of *Coleus aromaticus* (Roxb.) Benth. Leaves: Chromatography and NMR Analysis

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Coleus aromaticus (Roxb.) Benth. (Lamiaceae) is a species of semi-succulent perennial plant with recognized medicinal and nutritional relevance, widely employed in traditional medicine. While its aromatic fraction and essential oils have been extensively investigated, the non-volatile secondary metabolism of the plant remains poorly characterized. In particular, the free amino acids have never been investigated.

In this study, fresh leaves of *C. aromaticus* were treated with liquid nitrogen, ground, and subjected to different extraction procedures: hydroalcoholic maceration, maceration in ethyl acetate, and liquid-liquid partitioning yielding an organic phase in dichloromethane and a hydroalcoholic phase. The resulting fractions were analyzed by HPTLC and HPLC to define their metabolic profiles. In addition, the Bligh-Dyer method was applied to extract polar and non-polar metabolites, which were subsequently characterized by NMR spectroscopy.

Chromatographic and spectroscopic analyses revealed the presence of organic acids, polyphenols (notably flavonoids), and proteinogenic amino acids. The detection of both polar and non-polar metabolites provided a detailed chemical fingerprint of *C. aromaticus* leaves. In particular, the organic acids rosmarinic acid and caffeic acid were found to be the most abundant compounds, with concentrations of 88.89 mg/100 g and 49.66 mg/100 g, respectively. The flavonoids apigenin, luteolin and quercetin were also clearly identified, together with the free proteinogenic amino acids alanine, arginine, asparagine, aspartic acid, glutamic acid, glutamine, and serine. The most abundant amino acid was asparagine, with a concentration of 7.51 mg/100 g of matrix. This integrated approach offered a broader compositional overview of *C. aromaticus*, expanding its phytochemical profile beyond the well-documented essential oils.

These findings contribute to a deeper understanding of the non-volatile secondary metabolism of *C. aromaticus* and emphasize its potential as a source of bioactive metabolites with possible nutraceutical and pharmaceutical applications.



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sciforum-152123: Chemical composition and biotechnological potential of lichens from desert and coastal oases in Chile

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In northern Chile, such as the Atacama Desert and coastal fog oases, there is a highly specialized biota of lichens adapted to extreme conditions of aridity, UV exposure, and limited nutrients. This work consists of a literature review of the biotechnological potential of compounds present in lichens from arid ecosystems in Chile. Among the most representative families are Ramalinaceae, Pannariaceae, Physciaceae, Parmeliaceae and Cladoniaceae, whose species involved have secondary metabolites with important functional functions and biotechnological applications. Compounds such as tumidulin and ramaline derivatives have demonstrated antioxidant activity and significant antitumor activity in concentrations between 5 µg/mL and 50 µg/mL respectively in the Ramalinaceae family, with a protective role against oxidative stress. In humid microenvironments created by fog, the Pannariaceae family has been associated with the production of psoromic acid, which possess high enzyme inhibitory activity over HMG-CoA reductase (60 µg/mL; 65,18 to 74,81%) and AChE (10 µg/mL; 43,47%) and beneficial effects on free radicals. Physciaceae, adapted to develop on exposed substrates, produces depsidones and depsids with antioxidant activity and ROS-regulating activity. In Parmeliaceae, metabolites such as usnic acid and physiodic acid are antimicrobial and exhibit cytotoxic activity at multiple concentrations and bacteria species/cell lines, while Cladoniaceae provides compounds such as fumarprotocetric acid with anti-inflammatory and bactericidal activities with MIC values of 4.6 µg/mL in Gram (+) bacteria such as *Bacillus cereus* and *Bacillus subtilis*, and Gram (-) bacteria such as *Listeria monocytogenes*. These phytochemicals protect against radiation, desiccation and consumption by herbivores, being excellent candidates for the generation of pharmaceuticals, cosmetics and natural antioxidants. Combined taxonomic, chemical, and bioanalytical research reveals that the chemical diversity of desert lichens is strongly correlated with habitat and phylogeny. The conservation of lichen biodiversity in desert areas can be proposed as a strategy in biotechnological innovation and in the research of extreme environments.



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sciforum-152117: Chemometric Multivariate Analysis for Species Classification in the Genus *Baccharis* (Asteraceae)

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Within the genus *Baccharis* (Asteraceae), about 50 species collectively known as “Carquejas” are notable for their high content of essential oils and their widespread use in Brazilian folk medicine, particularly for their digestive, anti-inflammatory, and hepatoprotective properties. Despite this extensive use, only *Baccharis trimera* (Less.) DC. currently has an officially established quality control protocol in Brazil. This protocol, however, relies exclusively on morphological analysis, a restricted approach that is insufficient to ensure the rigorous quality standards required for commercially available products, such as capsules, extracts, and sachets. This study aimed to develop a chemometric exploratory and classification model using the MATLAB toolbox (version R2025a) to analyze hydroalcoholic extracts from five Carqueja species (*B. trimera*; *B. articulata* (Lam.) Pers.; *B. sagittalis* (Less.) DC; *B. junciformis* DC.; *B. pentaptera* (Less.) DC.). The dataset comprised 250 mid-infrared Fourier Transform spectroscopy spectra (4000–400 cm⁻¹), with 50 spectra per species. Principal Component Analysis (PCA) and Partial Least Squares - Discriminant Analysis (PLS-DA) were employed to construct the exploratory and classification models, respectively. PCA explained 98,0% of the total variance, allowing clear separation of the five *Baccharis* species using six principal components. The model with PLS-DA algorithm was built using the same dataset and evaluated through 10-fold Venetian Blinds cross-validation. It achieved a total explained variance of 88,9%, with an overall classification accuracy across classes of 90,0%, and specificity and sensitivity values of 90,0% and 71,0%, respectively, using four latent variables. The most relevant spectral regions contributing to the discrimination were located between 1750 cm⁻¹ and 750 cm⁻¹. Both models, the exploratory and the classification approaches, proved effective in evaluating and highlighting the differences among the *Baccharis* species, confirming the potential of chemometric tools as an innovative strategy for the quality control and regulatory monitoring of Carqueja-based products.



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sciforum-124883: Chlorogenic acid inhibits smooth muscle cell senescence and phenotypic switch to alleviate aortic dissection

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Background and aims: Cellular senescence and inflammation-mediated phenotypic switch in smooth muscle cell (SMC) are pivotal factors in the aortic degenerative remodeling and the development of aortic dissection. Chlorogenic acid (CGA), a natural polyphenolic compound of plant origin, exhibits remarkable anti-aging and anti-inflammation properties. However, the role of CGA in the aortic degenerative remodeling and aortic dissection remains elusive.

Methods: In this study, a BAPN (beta-aminopropionitrile)-induced aortic dissection model in vivo and DOX (doxorubicin)-induced cell senescence model in vitro were employed, in combination with activity-based protein profiling (ABPP) technology, to explore the mechanism by which CGA inhibits aortic dissection.

Results: The results revealed that CGA could prophylactically and therapeutically prevent BAPN-induced aortic dissection in mice, with reduced mice death and aortic diameter, inhibited aortic SMC senescence, inflammatory responses and phenotypic switch. Transcriptome sequencing of aortic tissues demonstrated that CGA treatment downregulated the expression of genes related to senescence and SMC synthesis, while upregulating the expression of contractile genes in aortic SMCs. These findings were further validated in DOX-induced senescent SMCs. Based on ABPP technology, a CGA chemical probe was utilized to exploring its protein targets, and Mettl3 was identified and verified as a potential target of CGA in senescent SMCs. Inhibition of Mettl3 using a specific inhibitor reduces the senescence and phenotypic transformation of SMCs in vitro. Concomitantly, Mettl3 specific inhibitor could also prophylactically and therapeutically prevent BAPN-induced aortic dissection in mice.

Conclusions: In summary, this study offers novel insights into halting the progression of aortic dissection and may facilitate the application of CGA in the prevention of aortic dissection.



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sciforum-152348: Cinnamaldehyde Analogues as antibacterial agents: A Study of Structure-Activity Relationship

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The rise of antimicrobial resistance (AMR) to the plethora of current antibiotics constitutes a major threat to public health, urging for the discovery of novel antibiotics through natural products. This study explores the potential of ten cinnamaldehyde analogues as novel antibacterial agents against model organisms, namely *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. Antibacterial activity and structure-activity relationships (SARs) were assessed using high-throughput screening (HTS) and minimum inhibitory concentration (MIC) assays, with ampicillin included as a standard control compound. Synergy was evaluated through checkerboard assays with ampicillin and neomycin. Hydroxylated cinnamaldehyde analogues, namely 1.2 and 1.3, exhibited enhanced bioactivity against *Escherichia coli* when compared to the parent compound (cinnamaldehyde). Most ketone derivatives resulted in minimal or reduced potency with the exception of 2.3 (MIC at 5mM with a 17.26% growth). Compounds 1.1, 1.2, 1.3 aldehydes exhibited an MIC (5 mM, 2.5 mM, 0.016 mM respectively) and adequate microbial growth inhibition (2.33-9.49%) for *Staphylococcus aureus*. Interestingly, ketones 2.3, 2.4 resulted in MICs at 5 mM with ~ 15% microbial growth. As for *Pseudomonas aeruginosa*, a similar trend of ketone inactivity was observed with none of them achieving more than 55.8% inhibition. The aldehyde group here presented better efficacy. Specifically, compounds 1.1, 1.2 with MIC = 5 mM and MIC = 2.5 mM respectively. Notably, compound 1.1 was able to achieve complete inhibition at the concentration of 5 mM. The importance of keeping the aldehyde core while strategically adding hydroxyl groups and bromine for antimicrobial efficacy was highlighted through SAR analysis. Synergistic effect trials with ampicillin and neomycin revealed mainly indifferent interactions, with cases of additive and synergistic effects related to potency alone.



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sciforum-151536: Comparative *in vitro* assessment of antibacterial activity of prepared Propolis ointment against common wound pathogens.

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Introduction:

Propolis, a resinous material collected by honeybees from plant exudates, possesses strong antimicrobial properties. However, its composition and potency vary geographically. Despite extensive research, few studies have directly compared its antibacterial efficacy with standard antibiotics. This study aimed to evaluate the antibacterial activity of Iraqi propolis and compare it with Fucidin® to assess its therapeutic potential.

Methods:

Propolis soft extract was obtained by maceration in 70% ethanol (1:10 w/v). Ethanolic extracts (5% and 10%) were prepared from the soft extract, and ointments (5%, 10%) were formulated with petroleum jelly, paraffin, wool fat, and stearyl alcohol. Physicochemical parameters (spreadability, viscosity, pH, stability) were evaluated. Antibacterial activity was assessed against *S. aureus*, *S. epidermidis*, *E. coli*, and *P. aeruginosa* using the Kirby–Bauer disk diffusion method, with Fucidin® as control. MICs for Gram-positive isolates were estimated from inhibition zone diameters, and results were statistically analyzed ($p < 0.05$). GC–MS was employed to identify volatile constituents not typically detected by HPLC, contributing to the antibacterial profile of Iraqi propolis.

Results:

Both ointments showed semi-stiff consistency, pseudoplastic behavior, and a pH of 5, suitable for topical use. They remained stable at 25 °C for 90 days and at –20 °C and 40 °C for 30 days. The 5% extract produced inhibition zones of 25 ± 0.81 mm (*S. aureus*), 21 ± 0.81 mm (*S. epidermidis*), 13.33 ± 1.24 mm (*E. coli*), and 12.75 ± 0.54 mm (*P. aeruginosa*), surpassing Fucidin® against Gram-negatives ($p < 0.001$) and showing comparable efficacy for Gram-positives ($p > 0.05$). Ointments showed smaller inhibition zones (15–18 mm), MIC was 1% for Gram-positive isolates. GC–MS revealed 20 volatile compounds.

Conclusion:

Iraqi propolis demonstrated potent antibacterial activity comparable to Fucidin®, with superior efficacy against Gram-negative bacteria. It represents a promising natural antimicrobial requiring further optimization and standardization.



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sciforum-147846: Comparative Assessment of Nigerian and Yemeni Garlic as Phospholipase A₂ (PLA₂) Inhibitors in Snakebite Envenomation Therapy

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Snakebite envenomation remains a significant medical challenge, particularly in tropical and subtropical regions. This study aimed to evaluate the inhibitory potential of *Allium sativum* (garlic) from Nigeria and Yemen against *Naja nigricollis* and *Echis ocellatus* venoms using both experimental and computational approaches. Fresh garlic samples were collected, authenticated, and extracted using cold methanol maceration to yield Nigerian and Yemeni methanol extracts (NME and YME, respectively). Their antisnake venom activities were assessed *in vitro* and *in silico*, with polyvalent antivenin (ASV) serving as the standard control. Comparative qualitative phytochemical screening was performed to identify secondary metabolites in both extracts. The results demonstrated significant ($p < 0.05$), concentration-dependent inhibition of venom phospholipase A₂ (PLA₂) activity. YME exhibited superior PLA₂ inhibitory activity (80.02 to 53.01%) compared to NME (72.51 to 38.20%) across concentrations ranging from 10.0 to 0.625 mg/mL. Furthermore, molecular docking of bioactive compounds identified in YME via HPLC and LC-MS/MS revealed strong binding affinities (−8.5 to −7.2 kcal/mol) to the active site of PLA₂, indicating potential inhibitory interactions. The selected compounds also exhibited favorable drug-likeness and pharmacokinetic (ADMET) profiles. In conclusion, the study provides scientific validation for the traditional use of *Allium sativum* in Nigeria and Yemen as an herbal remedy for snakebite envenomation, highlighting the promising anti-snake venom potential of Yemeni garlic through PLA₂ inhibition.



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sciforum-141302: Comparative study of the antioxidant activity of *Anthemis punctata* and *Anthemis maritima* extracts by DPPH assay

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The genus *Anthemis* (Asteraceae) is well known for its richness in bioactive secondary metabolites, particularly phenolic compounds, which are associated with notable antioxidant properties. Despite this interest, comparative data on the antioxidant activity of extracts from different *Anthemis* species remain limited, especially regarding the influence of solvent polarity. This study focuses on evaluating and comparing the antioxidant potential of dichloromethane and hexane extracts from the aerial parts of *Anthemis punctata* and *Anthemis maritima*.

In this study, we investigated the antioxidant potential of four extracts obtained from the aerial parts of two *Anthemis* species: *A. punctata* and *A. maritima*. The plant materials were successively extracted using hexane and dichloromethane, yielding ARP1H and ARP1D (*A. punctata*), and ARP2H and ARP2D (*A. maritima*). The antioxidant activity was evaluated by the DPPH radical scavenging assay, and IC₅₀ values were determined.

The results revealed notable differences according to both species and solvent polarity. The dichloromethane extract of *A. punctata* (ARP1D) showed the strongest antioxidant effect (IC₅₀ ≈ 80 µg/mL), followed by the dichloromethane extract of *A. maritima* (ARP2D, IC₅₀ ≈ 110 µg/mL). In contrast, hexane extracts (ARP1H and ARP2H) exhibited weaker antioxidant activity, as indicated by their higher IC₅₀ values.

Overall, this comparative study demonstrates that solvent polarity and plant species significantly influence antioxidant capacity, highlighting *A. punctata* dichloromethane extract as a promising natural source of antioxidant compounds.



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sciforum-152371: Comparative Study of the Antioxidant and Antidiabetic Activities of the Methanol and Hexane Oil Extract of Bitter Melon (*Momordica charantia*)

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Introduction: Several diseases are associated with oxidative stress caused by free radicals. Current research focuses on finding naturally occurring antioxidants and antidiabetic agents of plant origin in treating oxidative-stress-related diseases. This study investigated the antioxidant and antidiabetic activities of methanolic and n-hexane essential oil extracts of *Momordica charantia* (bitter melon). **Methods:** The oils from the seeds of *M. charantia* were extracted with methanol and n-hexane, respectively, and their chemical constituents were analysed and quantified by GC-MS analyzer. The antioxidant activities of both oil extracts were measured by 1, 1-diphenyl-2-picryl-hydrazyl (DPPH), Hydroxyl radical (OH), and nitric oxide (NO) scavenging assays, while the antidiabetic activities were determined *in vitro* using the α -amylase and β -glucosidase assays.

Results: The GC-MS analysis revealed that methanol and n-hexane extracts of *Momordica charantia* seed oil are abundant in fatty acids such as pentadecanoic acid, octadecanoic acid, and cyclocoeicosanetriluoroacetic acid, and they both significantly demonstrated profound antioxidant and antidiabetic activity comparable to the reference antioxidant compound (ascorbic acid) and reference antidiabetic compound (acarbose). The essential oil from the methanol extract caused better inhibition of DPPH (89.69%), OH (75.12%), and NO (74.19%) at the highest concentration (500 μ g/mL) investigated, despite both oils showing a dose-dependent antioxidant activity. The oils of the two solvents of *M. charantia* seeds also expressed dose-dependent inhibitory activity for α -amylase and β -glucosidase comparable to acarbose; however, the n-hexane oil extract demonstrated better antidiabetic activity for β -glucosidase (IC₅₀ = 29.89 $\pm$ 0.051 μ g/mL) compared to the methanolic oil extract (IC₅₀ = 58.59 $\pm$ 0.047 μ g/mL).

Conclusion: The results conclude that *M. charantia* seed oils are a good source of polyunsaturated fatty acids and afford an essential basis for the use of the oil in the treatment of oxidative-stress-related diseases like diabetes mellitus.



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sciforum-151711: Computational identification of Penduletin and Chrysosplenol D from *Artemisia annua* as potential natural inhibitors of AKT1 in cancer therapy

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Introduction

Metastases remain a leading cause of cancer-related death, often due to chemotherapy resistance linked to dysregulation of signaling pathways, including PI3K/Akt. AKT1 is a key driver of tumorigenesis, proliferation, and survival, making it an attractive therapeutic target. Natural compounds from plants are being explored as safe and effective agents in cancer therapy.

Methods

A total of 392 phytochemicals from *Artemisia annua* were screened for AKT1 inhibition. Molecular docking was carried out using InstaDock, and top hits were evaluated through ADMET profiling, PASS analysis, and 500 ns molecular dynamics (MD) simulations. Binding stability was further analyzed with Principal Component Analysis (PCA), Free Energy Landscape (FEL) mapping, and RMSD/RMSF analyses.

Results

Penduletin (docking score -9.4 kcal/mol) and Chrysosplenol D (-9.1 kcal/mol) showed strong binding within the ATP-binding region, forming key interactions with LEU156, GLY157, LYS158, VAL164, and ASP274. MD simulations confirmed complex stability, with average RMSD values of 0.63 nm for AKT1-Penduletin and 0.58 nm for AKT1-Chrysosplenol D, compared to 0.69 nm for apo AKT1. RMSF analysis revealed moderate flexibility of the AKT1 loop region (residues 110–140), which was slightly increased upon ligand binding (0.30 nm for Penduletin and 0.28 nm for Chrysosplenol D), suggesting stable but flexible interactions around the active site. Both compounds met drug-likeness criteria, showed favorable pharmacokinetics, and demonstrated antioxidant, anticarcinogenic, and antineoplastic potential in PASS analysis. FEL analysis indicated energetically stable binding states, supporting their inhibitory activity.

Conclusion

Penduletin and Chrysosplenol D demonstrated strong binding affinity and stable interactions with AKT1. These findings highlight *Artemisia annua* phytochemicals as promising leads for developing novel cancer therapies.



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sciforum-148330: Effect of Copaiba Oil on the Thoracic Aorta of Streptozotocin-induced Diabetic Rats

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Introduction: Diabetes mellitus (DM) is a chronic metabolic disorder associated with vascular complications, particularly cardiovascular disease. The use of natural compounds such as copaiba oil (*Copaifera* spp.) has gained attention due to its antioxidant and anti-inflammatory properties. This study aimed to evaluate the effects of copaiba essential oil (OEC) on the thoracic aorta of streptozotocin (STZ)-induced diabetic rats.

Methods: Forty male Wistar rats were randomly assigned to five groups: non-diabetic control (CT), non-diabetic + OEC 200 mg/kg (C200), diabetic control (DC), diabetic + OEC 100 mg/kg (D100), and diabetic + OEC 200 mg/kg (D200). Diabetes was induced using STZ (65 mg/kg, i.v.). OEC was administered orally for 20 days. Body weight, glycemia, heart weight, and thoracic aorta morphology were analyzed. Histological sections were stained and assessed for intima-media thickness and volume density (Vv%) of smooth muscle and collagen. ANOVA followed by Tukey's test was used for statistical analysis (p0.05).

Results: Diabetic groups showed significant weight loss and hyperglycemia compared to controls (p0.0001). Treatment with OEC did not reverse these metabolic changes. No significant differences were found in intima-media thickness or Vv% of collagen and smooth muscle between diabetic groups. However, OEC-treated diabetic groups showed a non-significant trend toward preserved intima-media thickness.

Conclusions: OEC (100 and 200 mg/kg) did not significantly improve glycemic control or vascular morphology in diabetic rats within 20 days. Nevertheless, its safety in normoglycemic animals and possible protective trend on vascular structure support further long-term studies at higher doses.



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sciforum-148331: Effects of Copaiba Oil on Myocardial Morphology in Streptozotocin-Induced Diabetic Rats

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Introduction: Diabetes mellitus is associated with cardiovascular complications, including structural and functional alterations of the myocardium. Copaiba oil (*Copaifera* spp.) has been traditionally used for its anti-inflammatory, antioxidant, and wound-healing properties. This study aimed to evaluate the potential cardioprotective effects of copaiba essential oil (OEC) on the myocardial morphology of diabetic rats.

Methods: Male Wistar rats (70 days old, n=40) were divided into five groups (n=8 each): control (CT), control treated with OEC 200 mg/kg (C200), diabetic control (DC), diabetic treated with OEC 100 mg/kg (D100), and diabetic treated with OEC 200 mg/kg (D200). Diabetes was induced by intravenous streptozotocin (65 mg/kg). OEC was administered daily by gavage for 18 days. After euthanasia, the hearts were collected, weighed, and processed for histological and stereological analyses. Parameters included cardiosomatic index and volume densities (Vv) of cardiomyocytes, collagen, and blood vessels. Statistical analysis was performed using ANOVA with Tukey's post-test (p0.05).

Results: Diabetic animals showed significantly reduced body and heart weights compared to controls (p0.001). However, no significant differences were observed among groups in cardiosomatic index or stereological parameters of cardiomyocytes, collagen, and vessels. Interestingly, OEC administration in diabetic rats was associated with worsened hyperglycemia, with final blood glucose levels exceeding those of untreated diabetic controls. No morphological evidence of cardioprotection or reduction of inflammatory infiltrates was detected.

Conclusion: Copaiba oil did not promote cardioprotective effects in this model of type 1 diabetes. On the contrary, it aggravated hyperglycemia in diabetic rats, while producing only mild hypoglycemic effects in controls. These findings highlight the need for caution regarding indiscriminate use of copaiba oil in diabetic patients and underscore the importance of further studies addressing dosage, administration, and chemical composition standardization to better clarify its cardiovascular effects.



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sciforum-133064: Emerging Trends in Herbal Drug Delivery: Innovations and Applications

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In recent years, herbal medicines have garnered worldwide attention from both people and researchers due to their aesthetic value, improved patient compliance, and significant therapeutic effects. Herbal drugs can be more effectively utilized by incorporating them into modern dosage forms. This can be achieved through the design of novel herbal ingredient drug delivery systems, which represent innovative approaches addressing the limitations of traditional drug delivery systems. Implementing novel drug delivery technologies in herbal medicine has the potential to enhance efficacy and reduce the side effects associated with various herbal compounds and herbs. These formulations offer several advantages over traditional methods, including improved solubility and bioavailability, reduced toxicity, controlled drug delivery, and protection of plant actives from degradation. Moreover, they exhibit drug-targeting properties that enhance selectivity, delivery precision, and overall effectiveness, often allowing for dose reduction. These advancements not only increase safety but also promote patient compliance. Various novel herbal drug delivery systems include liposomes, phytosomes, nanoemulsions, nanoparticles, ethosomes, and transferosomes, each offering unique benefits. For instance, liposomes and nanoparticles can encapsulate poorly water-soluble herbal extracts, enhancing their absorption and stability. Phytosomes improve the bioavailability of polyphenolic compounds, while nanoemulsions enhance skin penetration in topical applications. These systems not only protect active constituents from environmental degradation but also improve therapeutic indices by ensuring site-specific delivery. Furthermore, these technologies can be applied to both traditional herbal formulations and modern herbal products, bridging the gap between conventional herbal therapy and advanced pharmaceutical science. With continued research and development, novel herbal drug delivery systems are poised to revolutionize the way herbal medicines are administered, making them safer, more effective, and more acceptable to modern consumers.



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sciforum-151211: Engineering a Bacterial Platform for Efficient Expression of Histatin 5: A Promising Candidate for Antimicrobial Therapy

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Introduction: Antibiotic resistance remains a key medical challenge, highlighting the need for alternative antimicrobial agents. Antimicrobial peptides are promising candidates due to their broad activity and high selectivity. Histatins produced by salivary gland cells are notable for their fungicidal, bacteriostatic, wound-healing, and immunomodulatory properties. Recombinant production of histatins may offer a more feasible approach than chemical synthesis. This study aimed to develop a bacterial expression system for histatin 5 (Hst5), including cassette constructs designed to enhance expression.

Methods: Plasmids pH5 and p10xH5 were constructed using the pET30(a) vector. Cloning was performed in *E. coli* XL1-Blue, followed by plasmid purification and restriction analysis. Peptide expression was performed in *E. coli* BL21(DE3) with IPTG induction. Peptides were detected by PAGE and purified using SP-Sepharose ion-exchange chromatography. Cassette peptide was hydrolyzed with cyanogen bromide to release Hst5 monomers. Peptide concentration was determined by the Bradford assay. Antimicrobial activity was assessed against *E. coli* using agar diffusion assay.

Results: Both vectors encoding the monomeric and cassette Hst5 were obtained. Optimal induction conditions were established (200 μ M IPTG, 90 min), and Hst5 was eluted at 170–290 mM NaCl. Hydrolysis of the cassette form resulted in Hst5 monomers (280.7 μ g/mL). The recombinant peptide displayed pronounced antimicrobial activity comparable to ampicillin.

Conclusions: The results demonstrate the feasibility of producing biologically active Hst5 in a bacterial expression system. This approach offers a cost-effective strategy for generating histatins, supporting the development of novel therapeutics against resistant pathogens. This work was supported by the Ministry of Science and Higher Education of the Russian Federation in 2025 (Agreement No. 075-15-2025-464).



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sciforum-151809: Exploring *Calophyllum inophyllum* Phytoconstituents as ClpC1 Inhibitors for Combating Drug-Resistant Tuberculosis

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Introduction

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (Mtb), remains a major global health concern, further complicated by multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains that reduce the effectiveness of conventional therapies. ClpC1, a protease regulatory ATPase essential for Mtb survival, has emerged as a promising therapeutic target. Natural products such as cyclomarin A and ecumicin inhibit ClpC1 effectively, but their complex structures and poor pharmacokinetics restrict clinical application. *Calophyllum inophyllum*, a tropical plant with documented antimicrobial activity, may serve as a source of novel ClpC1 inhibitors.

Methods

In this study, 52 phytoconstituents from *C. inophyllum* were screened using *in silico* approaches including molecular docking, ADMET profiling, PAINS filtering, and biological activity prediction.

Results

Friedelin and Canophyllal showed strong binding affinity (−7.8 and −7.7 kcal/mol) toward ClpC1, superior to the control inhibitor HEPES (−3.7 kcal/mol), forming stable interactions with key residues. ADMET evaluation indicated favorable pharmacokinetics, high gastrointestinal absorption, and no toxicity alerts. Molecular dynamics simulations up to 500 ns confirmed stability, with both compounds exhibiting lower RMSD and RMSF values than free ClpC1. Principal component and free energy landscape analyses validate their stability.

Conclusion

Outcomes of the study highlighted Friedelin and Canophyllal as promising scaffolds for developing ClpC1-targeting anti-TB agents, meriting further experimental validation.



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sciforum-152198: Flavonoid Profile of BRS Violeta Grape Pomace Extract Obtained via Pressurized Liquid Extraction

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Grape pomace, generated during wine and juice production, retains nutrients and bioactive compounds, particularly phenolics. Flavonoids, the largest class of phenolics, exhibit antioxidant, antimicrobial, antitumor, and cardioprotective activities. Various extraction techniques have been studied to improve the recovery of these compounds. Pressurized Liquid Extraction (PLE) subjects a solvent to high pressure and temperature, below its critical point, enhancing the solubility and diffusion of bioactive compounds from solid or semi-solid matrices. This study aimed to determine the flavonoid profile of BRS Violeta grape pomace obtained by PLE. Pomace from juice production was dehydrated, milled (20–28 mesh), and extracted using 70% acetone at 10 MPa, a flow rate of 5 mL/min, for 30 minutes. The extracts were analyzed by HPLC-DAD for flavonoid identification and quantification. A total of 16 flavonoids were identified, with hesperidin (0.724 ± 0.006 mg/g), myricetin (0.655 ± 0.005 mg/g), naringenin (0.640 ± 0.001 mg/g), petunidin-3-glucoside (0.615 ± 0.009 mg/g), and procyanidin B2 (0.552 ± 0.001 mg/g) being the most abundant. Of nine anthocyanins analyzed, only two were detected, probably due to their extraction into the juice during processing. Results demonstrate the potential of PLE to recover flavonoids of pharmaceutical interest, particularly myricetin, which also exhibits anti-hyperglycemic activity. These findings indicate that BRS Violeta grape pomace is a promising source of bioactive compounds for health applications and metabolic disorder prevention. Despite the variety's widespread use in juice production, its pomace phenolic composition remains poorly studied, and this work contributes to filling this knowledge gap.



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sciforum-152302: From Computational Prediction to Behavioral Validation: Pharmacokinetic Profiling and Molecular Docking of Phytochemicals as Essential Stages Before Preclinical Testing in Alzheimer's Disease Models

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Rubus fruticosus L. phytochemicals represent a rich source of bioactive molecules with antioxidant, anti-inflammatory, and neuroprotective potential. These polyphenolic compounds enhance endogenous antioxidant enzymes such as superoxide dismutase and catalase, mitigating oxidative stress and potentially delaying cognitive decline. Their ability to stimulate α -secretase and inhibit β -secretase suggests interference with amyloid aggregation, a central process in Alzheimer's disease (AD) pathology.

Comprehensive in silico pharmacokinetic profiling (SwissADME, pkCSM, DEEP-pk) indicated high gastrointestinal absorption for all analyzed phytochemicals (p-coumaric acid: 91.12%, daidzein: 93.04%, 4-hydroxybenzoic acid: 77.49%, cinnamic acid: 94.02%, ferulic acid: 94.10%, guaiacol: 93.37%) and favorable blood-brain barrier permeability. Compounds exhibited logBB values from -0.315 to 0.205 and logPS values from -2.5 to -1.924, surpassing the respective thresholds (-1 and -3) and demonstrating superior predicted brain accessibility compared with galantamine (logPS = -3.022).

Compounds from *R. fruticosus* L. fractions displayed consensus LogP values 5 (1.05-2.24), TPSA $\leq 140 \text{ \AA}^2$ (29.46-70.67 $\text{\AA}^2$), and bioavailability scores of 0.85, except for daidzein and guaiacol (0.55). Unlike galantamine, these molecules are not predicted to be P-glycoprotein substrates, suggesting reduced efflux and improved CNS bioavailability. Compared with galantamine, the phytochemicals exhibited equal or higher predicted oral bioavailability (0.85) and full compliance with Lipinski, Veber, and Egan filters, with at most a single Muegge or Ghose rule violation. Predicted skin permeability values further support their systemic absorption potential.

To validate these predictions, 5xFAD mice (n = 40) were randomly assigned to three treatment groups (FT, FH, LH; n = 10 per extract, with 5 mice receiving 50 mg/kg and 5 receiving 100 mg/kg), a negative control group (NaCl, n = 5), and a positive control group treated with a standard AD medication, galantamine (n = 5). All treatments were administered via oral gavage for seven consecutive days and one hour prior to behavioral testing. Behavioral outcomes were assessed using standardized tests, and statistical analyses were performed to determine significance between groups (p < 0.05). Cognition, as well as anxiety- and depression-like behaviors, were evaluated using the Y-Maze, Open Field Test, Novel Object Recognition Test, Elevated Plus Maze, and Forced Swim Test. Behavioral assays revealed significant improvements in spatial and recognition memory, as well as anxiety- and depression-like behaviors. Distinct dose-dependent patterns were observed among the *R. fruticosus* L. fractions. FT exhibited an inverse dose-response, with the 50 mg/kg dose yielding superior cognitive performance, enhanced working and recognition memory, and reduced anxiety- and depression-like behaviors. In contrast, FH showed a classical dose-response, with higher doses (100 mg/kg) improving cognition, while lower doses increased general locomotor activity without enhancing cognition, likely reflecting general arousal rather than targeted exploration. These findings corroborate the computational predictions of BBB permeability and multitarget engagement, highlighting the translational relevance of this integrated approach.

This combined computational-experimental strategy highlights *R. fruticosus* L. phytochemicals as promising multitarget candidates for AD therapy and underscores the value of *in silico* modeling in prioritizing molecules with optimal CNS accessibility for preclinical investigation.



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sciforum-150082: From Hive to Health: Propolis Bioactives for Integrated Management of Trypanosomatid Infections

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Trypanosomatid parasites—particularly *Trypanosoma* and *Leishmania* species—are causative agents of several Neglected Tropical Diseases (NTDs) that impose substantial health and economic burdens on both humans and livestock across endemic regions. With no vaccines available and current chemotherapy is limited by toxicity, and widespread resistance. The need for sustainable, cross-species therapeutics is urgent. Guided by the One Health approach, which integrates human, animal, and environmental health, we investigated the antiparasitic potential of propolis-derived natural products.

Propolis is a complex resinous material produced by bees from local vegetation. It varies in composition depending on geographical and botanical sources. Using liquid chromatography coupled with high-resolution mass spectrometry (LC-MS), followed by principal component analysis (PCA), we profiled propolis samples collected from diverse geographical regions. This analysis revealed significant chemical diversity among samples. Orthogonal partial least squares (OPLS) regression analysis further identified bioactivity-associated markers: a butyrate ester of pinobanksin was linked to strong activity against *T. brucei*, while methyl ethers of chrysin and pinobanksin were associated with activity against *T. congolense*.

Our results indicate that the principal bioactive constituents across these samples are flavonoids—particularly phenolic compounds—which appear responsible for the observed broad-spectrum antiparasitic activity. Both crude and fractionated propolis extracts exhibited potent *in vitro* efficacy against *Trypanosoma* and *Leishmania* species, with low half-maximal effective concentrations (EC₅₀) and no detectable cytotoxicity to mammalian cells. Moreover, these compounds retained activity against drug-resistant strains, including diamidine-, arsenical-, and phenanthridine-resistant *T. brucei*, as well as miltefosine-resistant *L. mexicana*.

Altogether, these findings highlight propolis as a promising reservoir of flavonoid-based compounds for the rational development of safe, sustainable, and cross-species drugs targeting trypanosomatid diseases. This work supports a One Health-aligned strategy for integrated disease control and natural product drug discovery.



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sciforum-151613: Functional Hydrogels Fabricated via 4D Printing – Synthesis and Evaluation of Responsive Properties

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In this study, functional hydrogels were developed using advanced 4D printing technology, enabling the design of materials capable of dynamically responding to environmental stimuli. This approach allowed the fabrication of structures with programmable changes in shape and properties triggered by external factors such as temperature and humidity.

The obtained hydrogels were subjected to comprehensive characterization, including morphological analysis, evaluation of swelling and shrinkage behavior under varying conditions, structural stability, and mechanical performance. The results demonstrated that the use of 4D printing enables precise control over the architecture of hydrogel structures and provides the ability to engineer tailored responsive functionalities. Furthermore, correlations were identified between the hydrogel composition and the kinetics of their response, offering possibilities for designing materials adapted to specific biomedical or engineering applications.

The findings confirm that the developed hydrogels hold significant potential in areas such as regenerative medicine, drug delivery systems, and material engineering, where adaptability to changing environmental conditions is crucial. This work highlights the role of 4D printing as a powerful tool for the creation of intelligent materials with dynamic and customizable properties.

This research was carried out within the SMART-MAT Functional Materials Science Club of the Faculty of Materials Engineering and Physics at Cracow University of Technology (section SmartMat) and as part of the project entitled, „Functional hydrogels obtained by using 4D printing” financed by the FutureLab organization operating at Cracow University of Technology.



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sciforum-151986: Grape Antioxidant Dietary Fibre Modulates Apoptosis-Autophagy Balance via Bcl-2/Beclin-1 Axis in Healthy Colon

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Introduction:

Apoptosis and autophagy are essential for epithelial homeostasis and defense against stress in the colon, with the Bcl-2/Beclin-1 axis acting as a regulatory switch. Dietary bioactives, particularly grape-derived polyphenols and fibers, can modulate these pathways. Grape Antioxidant Dietary Fiber (GADF), derived from red grape pomace (*Vitis vinifera*, var. Cencibel), combines insoluble fiber with polyphenols, mainly high molecular weight proanthocyanidins. This study evaluated GADF's effect on apoptosis and autophagy regulation in the proximal colon of healthy rats.

Methods:

Male Wistar rats were fed either a control diet or a GADF diet (5% w/w replacing cellulose in an isoenergetic diet) for four weeks. Following euthanasia, apoptosis and autophagy were evaluated in proximal colonic mucosa by immunohistochemistry, Western blotting, and caspase activity assays.

Results:

GADF reduced intrinsic apoptosis, as shown by lower TUNELlabelling index (−56.1%, p0.0001) and decreased caspase-9 and caspase-3 activities (−56.5% and −64.5%, respectively, p0.0001). Caspase-8 was unaffected indicating no effect on the extrinsic pathway. The Bax/Bcl-2 ratio decreased (−22.2%, p0.001), supporting mitochondrial stability. Concurrently, autophagy was activated with Beclin-1 (+70.2%) and LC3B (+35.3%) upregulated (for both, p0.001), while p62/SQSTM1 decreased (−44.2%, p0.01). Beclin-1 and LC3B correlated inversely with apoptosis markers, whereas p62/SQSTM1 showed positive correlation.

Conclusions:

GADF modulates the apoptosis-autophagy balance in the healthy colon through regulation of the Bcl-2/Beclin-1 axis, which suggests enhanced autophagic activity and promotes cellular survival. GADF emerges as a promising dietary component to support gut barrier integrity while offering a sustainable option for functional food innovation.

Spanish patents registered under the numbers 2259258 and 2130092

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sciforum-142587: Hepatoprotective Effect of *Curcuma longa* Aqueous Extract in Cadmium-induced Toxicity in Wistar Rats

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Introduction: Cadmium (Cd) is one of the major occupational and environmental toxicants, that poses serious risks to metabolic health and liver functions. This study was designed to evaluate the protective effects of aqueous extract of *Curcuma longa* against cadmium-induced liver damage, blood glucose imbalance and lipid profile disruptions in male Wistar albino rats.

Method: Fresh rhizomes of *Curcuma longa* were bought in the market and identified by a Botanist with voucher number (UNH/05/0223). They were washed, peeled and crushed and soaked with water. This was allowed to stand for a while and the sieved out to obtain the aqueous extract. A total of 42 rats were divided into 6 groups comprising of 7 each, which are: normal control, untreated cadmium group (4 mg/kg), treatment control (400 mg/kg turmeric), and three treatment groups given: low (100 mg/kg), mid (200mg/kg) and high (400 mg/kg) doses of turmeric extract. After 21 days of simultaneous cadmium induction and treatment, the rats were fasted overnight before blood was collected through the retro-orbital sinus for biochemical analyses.

Results: Phytochemical results showed the presence of these compounds in mg/100 g- alkaloids: 97.23 ± 0.68 , flavonoids: 34.00 ± 2.00 , terpenoids: 37.00 ± 3.60 , steroids: 3.38 ± 0.18 , reducing sugar: 26.66 ± 1.45 , phenolics: 870.00 ± 25.19 . Treatment with *Curcuma longa* extract showed a significant ($p = 0.05$) improvement in the Cd-induced disruptions in biochemical parameters most especially at mid and high doses by lowering liver enzyme markers; aspartate aminotransferase (AST), lactate dehydrogenase (LDH) as well as direct bilirubin. There was also a marked decrease in blood glucose and TAG levels with slight improvement in total cholesterol (TC), low density lipoprotein (LDL) and high density lipoprotein (HDL) when compared with the untreated group.

Conclusion: Therefore, it is concluded that aqueous extract of *Curcuma longa* possesses strong hepatoprotective and metabolic benefit, offering potential as a natural therapeutic agent against Cd-induced toxicity.



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sciforum-152018: Identification of Cyclocurcumin and Curcumin Analogues as Potential MMP13 Inhibitors: Network Pharmacology and Computational Study

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Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterized by persistent synovial inflammation, cartilage degradation, and progressive joint dysfunction. Conventional therapies, while effective in slowing disease progression, are limited by adverse effects, incomplete remission, and high costs. Natural products, such as *Curcuma longa* (turmeric), offer a promising alternative due to their anti-inflammatory, antioxidant, and multi-target pharmacological properties. In this study, a network pharmacology and computational approach was employed to investigate the multi-target therapeutic potential of *Curcuma longa* against RA. A curated library of non-toxic, drug-like phytochemicals with reported anti-RA activity was developed through data mining and filtered using ADMET screening, yielding 111 compounds. Differentially expressed genes (DEGs) associated with RA were identified via meta-analysis of synovial tissue microarray datasets GSE55457 and GSE55235, resulting in 1,473 DEGs. Gene set enrichment analysis (GSEA) revealed key RA-associated pathways, and a protein-protein interaction (PPI) network analysis identified 31 hub genes. Compound-target mapping highlighted significant interactions between *Curcuma longa* phytochemicals and RA-associated hub genes, with MMP13 emerging as a central therapeutic target due to its critical role in extracellular matrix degradation, cartilage erosion, and joint destruction. Molecular docking studies demonstrated strong binding affinities (-8 kcal/mol) of lead compounds, including cyclocurcumin, curcumin, and (1E,4E)-1-(4-hydroxy-3-methoxyphenyl)-5-(4-hydroxyphenyl)-1,4-pentadiene-3-one, to MMP13, mediated via hydrogen bonding and hydrophobic interactions. Molecular dynamics (MD) simulations over 200 nanoseconds confirmed the stability of these ligand-protein complexes, supporting their potential inhibitory effects on matrix degradation pathways. Overall, this study provides mechanistic insights into the multi-target, multi-pathway modulation of RA by *Curcuma longa* phytochemicals. Cyclocurcumin and curcumin derivatives are highlighted as promising candidates for further in vitro and in vivo validation, paving the way for their development as adjunct or alternative therapeutic agents in RA management.



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sciforum-151395: In vivo investigation of the wound healing efficacy of *Tecoma undulata* (Sm.) Seem., and *Jathyadi Thailam* herbal ointment in Swiss albino mice.

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Background:

Preliminary phytochemical analysis of the hydroalcoholic extract of *Tecoma undulata* (Sm.) Seem. revealed a high flavonoid content (88.66 ± 0.57 QE/g), suggesting wound-healing potential. To further elucidate its therapeutic efficacy, ointment formulations containing 5% and 10% of the extract were developed using *Jathyadi Thailam* as a herbal base (oil) and evaluated for wound-healing activity in Swiss albino mice.

Methods:

The wound-healing potential of the formulations was assessed using burn and excision wound models. The ointments were evaluated for their physicochemical properties, including pH, spreadability, viscosity, and stability. Parameters, including wound contraction rate, epithelialization time, collagen deposition, and tensile strength, were measured. Comparative assessments were conducted between topical and oral administration, with standard povidone-iodine ointment serving as the standard reference.

Results:

Both 5% and 10% formulations complied with standard physicochemical criteria and demonstrated significant wound-healing activity ($p < 0.001$) in both models compared to the control. Enhanced wound contraction, shortened epithelialization period, and increased tensile strength were observed, particularly in the burn wound model. Topical application produced superior results relative to oral administration.

Conclusion:

The hydroalcoholic extract of *T. undulata*, when formulated with *Jathyadi Thailam*, exhibits pronounced wound-healing efficacy, especially in burn wound management. These findings support its potential as a safe, natural, and effective topical therapeutic agent for treating burn injuries.



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sciforum-152327: Inhibitory Actions of Ethanolic Fraction of *Sida linifolia* L. Leaves on Erectile Dysfunction-Relevant Enzymes in Male Rat Penile Tissue Homogenates: An *ex-vivo* and *in-silico* Approach

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Erectile dysfunction (ED) is a prevalent male sexual disorder frequently associated with impaired nitric oxide signaling, heightened oxidative stress, and the dysregulation of key enzymes such as acetylcholinesterase, arginase, phosphodiesterase-5 (PDE-5), and angiotensin-I converting enzyme (ACE). Limitations of current pharmacotherapies, including side effects and incomplete efficacy, have spurred interest in plant-derived bioactive compounds as alternative or complementary treatments. Although *Sida linifolia* is traditionally used for managing reproductive and inflammatory conditions, its mechanism of action remains unclear. This study explored the propensity of the ethanolic fraction of *S. linifolia* leaves (EtOHFSL) to inhibit enzymes linked to erectile dysfunction in rat penile tissue homogenate. Enzyme inhibition assays were conducted using rat penile tissue homogenates, while phytochemical constituents were identified using gas chromatography coupled with flame ionization detection (GC-FID) and supported by high-performance liquid chromatography (HPLC) profiling to confirm compound composition. Molecular docking studies (MDS) were performed using AutoDock Vina. Identified compounds in EtOHFSL included epicatechin, flavone, rutin, kaempferol, lunamarin, naringenin, ellagic acid, quercetin, and chlorogenic acid. EtOHFSL demonstrated moderate, concentration-dependent inhibition of PDE5, arginase, ACE, and AChE, with IC₅₀ values ranging from 0.66–0.84 mg/mL, which were compared cautiously with the respective pure reference inhibitors (sildenafil, L-NOHA, captopril, and galantamine) for reference purposes only. Molecular docking of experimentally confirmed phytochemicals such as epicatechin, rutin, kaempferol, lunamarin, and ellagic acid revealed strong binding affinities to ED-related enzymes. The in-vitro results corroborated in-silico molecular docking predictions, suggesting consistent inhibitory trends. In-silico ADMET predictions further indicated acceptable pharmacokinetic and toxicity profiles for most compounds. These preliminary findings suggest that *S. linifolia* contains bioactive constituents with enzyme modulatory potential against ED-related targets; however, further purification, isolation of active principles, and in-vivo validation are required to substantiate any therapeutic claims.



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sciforum-152122: Integrative Transcriptomics and In Silico Screening Identify Withaferin A as a Potential PSMB7 Inhibitor in Ovarian Cancer

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Serous ovarian cancer (SOC) is among the most aggressive gynecological malignancies, with high mortality due to late diagnosis, therapeutic resistance, and frequent relapse. Identification of novel molecular targets and natural inhibitors is urgently needed to improve treatment outcomes. This in silico study integrated transcriptomic data to identify hub genes in SOC and evaluated phytochemicals as potential inhibitors of the prioritized target protein PSMB7 via molecular docking and ADMET analysis. A meta-analysis of three GEO datasets (GSE27651, GSE36668, GSE54388) identified differentially expressed genes using a $\log_2$ fold-change threshold of ≥ 2 or ≤ -2 . Enrichment analysis with Enrichr revealed pathways associated with transcriptional regulation and DNA repair. A protein-protein interaction network constructed in Cytoscape and analyzed using CytoHubba, CentiScape, and MCODE identified hub genes including PSMD13, PSMC3, UBC, UBB, PSMD7, and PSMB7. Based on literature, PSMB7 was prioritized. Its crystal structure (PDB ID: 5LEL, chain A) was prepared by removing water molecules, adding hydrogens, and assigning charges. A library of phytochemicals from PubChem was energy-minimized and docked using AutoDock Vina, and ADMET properties were predicted using SwissADME and pkCSM. Withaferin A (PubChem CID: 265237) showed the strongest binding affinity (-9.265 kcal·mol⁻¹) and stable interactions in the catalytic pocket, with moderate solubility, favorable drug-likeness, and low predicted toxicity. Literature reports Withaferin A as a proteasome inhibitor capable of inducing apoptosis and cell cycle arrest, inhibiting angiogenesis and metastasis, and exerting anti-cancer effects in ovarian and other cancers. Molecular dynamics simulation over 200 ns confirmed the stability of the ligand-protein complex. Future validation will involve in vitro assays on ovarian cancer cell lines to confirm cytotoxicity, apoptosis, proteasome inhibition, and anti-metastatic effects, followed by in vivo studies in xenograft and orthotopic mouse models to assess pharmacokinetics, efficacy, and safety. These studies will provide essential experimental confirmation of Withaferin A as a natural inhibitor of PSMB7 in SOC.



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sciforum-148117: Leveraging Data-Driven AI to Explore Plant-Based Compounds for Neuroinflammation and Inflammatory Receptor Modulation via Polypharmacology

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Polypharmacology has emerged as a promising approach in modern drug discovery, allowing researchers to address the complex interplay of multiple biological pathways underlying disease mechanisms. In this study, advanced artificial intelligence (AI)-based tools were applied to evaluate the therapeutic potential of *Cyamopsis tetragonoloba*, a medicinal plant traditionally recognized for its anti-inflammatory activity, in the context of inflammation and neuroinflammation. By integrating AI-driven network pharmacology with protein-protein interaction analyses, AKT1 (protein kinase B alpha) was identified as a pivotal target that mediates the plant's pharmacological effects. This finding suggests a central role of AKT1 in modulating inflammatory signaling pathways.

To further explore these insights, molecular docking experiments were conducted using bioactive constituents derived from *Berberis aristata*, another well-documented medicinal plant with anti-inflammatory relevance. The docking studies focused on critical proteins involved in inflammatory processes, including AKT1, PTGS2, STAT3, PPARG, SIRT1, and MAPK1. Several compounds demonstrated strong binding affinities, in some cases comparable to or surpassing those of clinically approved anti-inflammatory drugs. Such results not only validate the computational predictions but also point to the potential of these plant-derived molecules as viable therapeutic candidates.

Overall, the findings highlight the value of combining AI technologies with polypharmacological strategies to accelerate the discovery of plant-based therapies. By identifying key molecular targets and validating compound interactions, this integrated approach offers new opportunities for developing effective treatments for inflammatory and neuroinflammatory disorders, while bridging traditional medicinal knowledge with modern computational drug discovery.



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sciforum-147248: Mechanistic evaluation of anti-inflammatory and antimicrobial properties of selected medicinal Plants

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Chronic inflammation and oxidative stress are major factors to the development and progression of degenerative, autoimmune and musculoskeletal diseases. The persistent creation of reactive oxygen species (ROS) and protracted inflammatory reactions cause cellular damage, lipid peroxidation, and DNA instability, demanding safer and more effective therapeutic alternatives to current medications. Traditional medicines describe various medicinal plants for treating inflammatory diseases their pharmacological qualities remain unknown. Hydroalcoholic extracts of *Aloe barbadensis* Mill., *Chrysanthemum indicum* L., *Commiphora mukul* Engl., *Convolvulus scammonia* L., *Ipomoea turpethum* L., and *Merendera persica* Boiss. was extracted using Soxhlet and tested for phytochemical composition, antioxidant potential, DNA protective effects, anti-inflammatory, antimicrobial activity and safety. Phytochemical screening revealed the presence of flavonoids, phenolics, carbohydrates, and alkaloids, suggesting a high concentration of bioactive metabolites. Antioxidant ability was determined using DPPH, ABTS, FRAP, nitric oxide scavenging, and malondialdehyde (MDA) tests, which revealed significant free radical neutralisation and prevention of lipid peroxidation. Among the extracts examined, *A. barbadensis* showed considerable activity in DPPH and FRAP assays, while *Convolvulus scammonia* showed significant activity in ABTS and nitric oxide scavenging assays. *C. indicum* had the lowest amounts of MDA, indicating excellent lipid peroxidation inhibition. Furthermore, *C. scammonia* proved very efficient in preventing protein denaturation. *A. barbadensis* showed strong antimicrobial activity against *Escherichia coli* at a concentration of 10 µg/mL. The FTIR study also identified hydroxyl, carbonyl, and phenolic functional groups that are related with antioxidant and anti-inflammatory bioactivity. In conclusion, the findings give scientific support to the traditional usage of these herbs and emphasise their potential, natural and multi-targeted therapeutic agents for oxidative stress and chronic inflammation, notably in arthritis and associated diseases.



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sciforum-147163: Nanoparticle Systems for Improved Delivery of *Plectranthus*-Derived Abietane Diterpenoids in Breast Cancer Therapy

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Nanoparticles (NPs) have become key tools in modern drug delivery, especially when used alongside natural compounds. This combination can improve how drugs are absorbed and directed to specific targets in the body. Benefits include higher drug loading, controlled and sustained release, longer presence in the bloodstream, and reduced side effects. These advantages contribute to safer and more efficient therapies.

Among the various nanoparticle types, gold nanoparticles (AuNPs) stand out due to their easy production, strong stability, and unique physical and chemical traits. These properties make them excellent carriers for both drugs and genetic material, especially in cancer-related applications.

One group of natural compounds with promising anticancer activity is the abietane diterpenoids, such as 7 α -acetox-6 β -hydroxyroyleanone (**Roy**), found in *Plectranthus* species. Despite their potential, their clinical use is limited by poor water solubility and low bioavailability. To overcome these issues, **Roy** and one **Roy**-esterified derivative were incorporated into gold nanoparticle-based systems.

These nanoformulations were evaluated for characteristics like particle size (29.37 nm), polydispersity index (PDI, 0.399), surface charge (zeta potential, -6.84), and drug encapsulation efficiency (79.4%). In vitro experiments using breast cancer cell lines (MDA-MB-231, 4T1, and MCF7) showed that **Roy**-loaded AuNPs had significantly stronger anticancer effects than **Roy** alone or unmodified AuNPs. Notably, these systems also demonstrated selectivity, affecting cancer cells while sparing healthy human dermal fibroblasts (HDFs), suggesting strong potential for targeted cancer therapy. These results represent meaningful progress in the development of innovative drug delivery systems for cancer therapy.



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sciforum-146453: Nanostructured lipid carriers for enhanced oral bioavailability and antibacterial efficacy of curcumin against multidrug-resistant pathogens

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Background: Poor solubility and limited oral bioavailability restrict the clinical translation of curcumin despite its well-documented antibacterial and anti-inflammatory activity. Nanostructured lipid carriers (NLCs) offer a promising strategy to overcome these barriers by improving stability, gastrointestinal absorption, and therapeutic delivery.

Methods: Curcumin-loaded NLCs were prepared using hot homogenization and ultrasonication, with glyceryl monostearate as solid lipid and oleic acid as liquid lipid. Particle size, zeta potential, and entrapment efficiency were determined by dynamic light scattering and HPLC. In vitro release was studied under simulated gastric and intestinal conditions. Antibacterial activity was tested against MDR *Staphylococcus aureus* and *Escherichia coli* using MIC/MBC assays and biofilm inhibition models. Pharmacokinetic studies were conducted in Wistar rats following oral administration.

Results: Optimized curcumin-NLCs exhibited a mean particle size of 121 ± 8 nm, zeta potential of -32 mV, and entrapment efficiency of 89%. Controlled release demonstrated sustained drug release over 24 h. Antibacterial assays revealed significant improvement in potency, with MIC values reduced fourfold compared to free curcumin. Biofilm inhibition reached 73% at sub-MIC concentrations. Pharmacokinetic analysis showed a 5.2-fold increase in oral bioavailability, with peak plasma concentrations achieved at 3 h post-administration.

Conclusion: Curcumin-loaded NLCs significantly enhance oral bioavailability and antibacterial efficacy, representing a robust drug delivery platform for repositioning natural compounds against multidrug-resistant infections. These findings highlight the potential of lipid nanocarriers in medicinal chemistry and pharmaceuticals for developing next-generation therapeutic formulations.



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sciforum-146037: New Zealand Blackcurrant Anthocyanins Attenuate TNF- α -Induced PAI-1 Levels in Airway Epithelial Cells: Implications for Asthma Therapy.

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Introduction: Asthma is a chronic, inflammatory respiratory disease affecting millions worldwide, with increasing prevalence and substantial economic impact projected by 2050. Central to asthma pathogenesis are airway remodeling and inflammation, processes in which Plasminogen Activator Inhibitor-1 (PAI-1) acts as a major contributor by promoting extracellular matrix accumulation and fibrosis. Anthocyanins exhibit strong antioxidant and anti-inflammatory activities; however, their effects on airway remodelling have not been studied to date.

Methods : This study investigated the anti-inflammatory potential of New Zealand Blackcurrant (NZBC) anthocyanins in BEAS-2B bronchial epithelial cells. BEAS-2B cells' viability was assessed using the Methyl Thiazolyl Tetrazolium (MTT) assay to determine a non-cytotoxic concentration. Cells were pretreated with NZBC anthocyanins prior to TNF- α stimulation and then PAI-1 levels were quantified using ELISA.

Results: MTT assay revealed significant cytotoxicity at concentrations above 50 μ g/mL, confirming 50 μ g/mL as a safe dose for further analysis. Pretreatment with NZBC anthocyanins significantly reduced PAI-1 levels in TNF- α -stimulated cells (Control: 28,958 $\pm$ 2,485 vs. ACN: 14,360 $\pm$ 1,148; n = 3), as measured by ELISA.

Conclusion: These findings suggest a protective effect against the pro-fibrotic state. The outcomes underscore the therapeutic potential of anthocyanins as adjunctive agents in asthma therapy, particularly in targeting oxidative stress and airway remodeling pathways. Further studies are warranted to explore their clinical relevance and therapeutic efficacy.



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sciforum-151621: Non-invasive anti-wrinkle electrospun nanofiber patch containing physalis stem cells extract and liposomal vitamin C

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Plant-derived antioxidants play a critical role in protecting against skin ageing-related oxidative damage, yet their therapeutic use is limited by instability, low absorption, reduced bioavailability, and restricted skin penetration. Nanocarriers such as coaxial electrospun nanofibers provide a promising delivery system, enhancing stability and penetration while enabling synergistic effects. In this study, we investigated a novel approach combining liposomal vitamin C, a widely used antioxidant, with Physalis extract enriched in secondary metabolites obtained through tissue culture techniques.

Physalis stem cell cultures were successfully established and treated with elicitors to boost metabolite production, where jasmonic acid (JA) proved the most effective compared to salicylic acid (SA). Liposomal vitamin C was formulated by thin-film hydration and characterized using electron microscopy, revealing nanosized vesicles with an average diameter of 250 nm, a zeta potential of -3.0 ± 0.5 mV, and a polydispersity index (PDI) of 0.23 ± 0.02 , confirming good stability and homogeneity. Both components were incorporated into coaxial electrospun nanofibers, which exhibited uniform morphology, smooth surface, and nanoscale dimensions as confirmed by scanning electron microscopy.

In vivo testing on a mouse dorsal skin model showed that the nanofiber patch significantly enhanced antioxidant defense. Elevated superoxide dismutase (SOD) and glutathione (GSH) levels, alongside reduced malondialdehyde (MDA), indicated strong protection against lipid peroxidation and oxidative stress.

Collectively, these findings highlight that JA-elicited Physalis metabolites, when co-delivered with liposomal vitamin C in a coaxial nanofiber patch, represent a novel and effective therapeutic strategy for improving antioxidant efficacy and preventing oxidative stress-induced skin damage.



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sciforum-149884: Phytochemical Analysis, Quantification of Flavonoids and Phenols, and Assessment of Anti-Tubercular Activity of *Citrus jambhiri* Fruit Peel Extract

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Introduction:

Tuberculosis (TB) remains a global health concern, prompting the exploration of natural products for novel therapeutics. Citrus fruit peels, often discarded as waste, are rich in bioactive compounds with potential antimicrobial and antioxidant properties.

Methods:

This study investigated the extraction, phytochemical profiling, and anti-tubercular potential of *Citrus jambhiri* fruit peel. The dried and powdered peel was extracted by maceration with 95% ethanol for 72 hours at room temperature with intermittent shaking. The extract was filtered and concentrated under reduced pressure to yield a semi-solid residue. Phytochemical screening was performed using standard qualitative tests. Total phenolic content (TPC) was determined by the Folin–Ciocalteu method, where 1 mL of extract (1 mg/mL) was mixed with 5 mL of 10% Folin–Ciocalteu reagent and 4 mL of 7.5% sodium carbonate. After 30 minutes, absorbance was measured at 765 nm, using gallic acid as a standard. Total flavonoid content (TFC) was determined by the aluminium chloride colorimetric assay, mixing 1 mL of extract with 4 mL of distilled water, 0.3 mL of 5% sodium nitrite, 0.3 mL of 10% aluminium chloride, and 2 mL of 1 M sodium hydroxide. Absorbance was measured at 510 nm with quercetin as standard. Anti-tubercular activity was evaluated against *Mycobacterium tuberculosis* H37Rv using the Microplate Alamar Blue Assay (MABA), with results expressed as minimum inhibitory concentration (MIC).

Results:

The extract showed the presence of alkaloids, flavonoids, tannins, phenols, terpenoids, and saponins. Quantitative analysis revealed TPC of 7.66 mg GAE/g and TFC of 10.76 mg RE/g. The extract exhibited potent anti-tubercular activity with an MIC of 25 µg/mL.

Conclusion:

Citrus jambhiri fruit peel, rich in polyphenols and flavonoids, demonstrates promising anti-tubercular potential, supporting its use as a natural source for lead molecule development in TB therapy.



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sciforum-151974: Phytochemical Analysis, Quantification of Flavonoids and Phenols, and Assessment of Anti-Tubercular Activity of *Citrus jambhiri* Fruit Peel Extract

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Introduction:

Tuberculosis remains a global health challenge, and natural products are being explored as alternative sources for novel therapeutics. Citrus fruit peels, often discarded as waste, are rich in bioactive compounds with potential antimicrobial effects.

Methods:

Preliminary phytochemical screening of the peel extract was performed using standard qualitative tests. Total phenolic content was quantified by the Folin–Ciocalteu method, while total flavonoid content was estimated using the aluminium chloride colorimetric assay. Anti-tubercular activity was evaluated against *Mycobacterium tuberculosis* H37Rv strain using Microplate Alamar Blue Assay (MABA), with results expressed as minimum inhibitory concentration (MIC).

Results:

The extract revealed the presence of alkaloids, flavonoids, tannins, phenols, terpenoids, and saponins. Quantitative analysis revealed that the ethyl acetate extract had the highest levels of total phenolic content (7.66 mg gallic acid equivalents per gram) and total flavonoid content (10.76 mg rutin equivalents per gram), suggesting strong antioxidant potential. For anti-tubercular testing, the Microplate Alamar Blue Assay (MABA) was employed—a reliable, colorimetric method for evaluating inhibition of *M. tuberculosis*. Both extracts exhibited promising activity, with a minimum inhibitory concentration (MIC) of 25 µg/ml, indicating potential anti-TB action.

Conclusion:

Citrus jambhiri fruit peel extract is rich in polyphenols and flavonoids and displays promising anti-tubercular activity. These findings highlight its potential as a natural source of lead molecules for anti-tubercular drug discovery. Further isolation and mechanistic studies are recommended.



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sciforum-148327: Phytochemical Profiling and Multi-Target Pharmacological Potential of *Peganum harmala* Seed Extract

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Introduction: Medicinal plants remain a promising reservoir of bioactive compounds with therapeutic potential against chronic and infectious diseases. *Peganum harmala* L. (Zygophyllaceae), commonly known as Syrian rue, is widely used in traditional medicine for its antitumor, antimicrobial, and anti-inflammatory properties, primarily due to its rich alkaloid profile (harmine, harmaline, and β -carbolines). However, systematic pharmacological validation of its bioactivity against contemporary health challenges is still limited.

Methods: Ethanolic extracts of *P. harmala* seeds were prepared via Soxhlet extraction and subjected to GC–MS analysis for phytochemical profiling. In vitro antioxidant potential was assessed using DPPH and FRAP assays, while antibacterial efficacy was evaluated against multidrug-resistant (MDR) strains of *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa* using agar well diffusion and MIC determination. Anti-inflammatory activity was examined via protein denaturation and membrane stabilization assays. Cytotoxicity was analyzed on HepG2 and MCF-7 cell lines using MTT assays.

Results: GC–MS revealed the presence of 22 major phytoconstituents, including harmine, harmaline, vasicine, and quinazoline derivatives. The extract demonstrated strong radical scavenging activity ($IC_{50} = 38.6 \mu\text{g/mL}$) and ferric reducing power ($420 \mu\text{mol Fe}^{2+}/\text{g extract}$). Potent antibacterial activity was observed with inhibition zones up to 22 mm against MDR *S. aureus*, with MIC values as low as $125 \mu\text{g/mL}$. The extract significantly reduced protein denaturation (67%) and stabilized red blood cell membranes (71%), suggesting robust anti-inflammatory effects. MTT assays revealed selective cytotoxicity, with IC_{50} values of $48 \mu\text{g/mL}$ for HepG2 and $62 \mu\text{g/mL}$ for MCF-7, while sparing normal fibroblast cells.

Conclusion: *Peganum harmala* seed extract represents a pharmacologically rich candidate for drug discovery pipelines targeting oxidative stress, inflammation, antimicrobial resistance, and cancer. Further in vivo validation and mechanistic studies are warranted to translate its traditional use into modern therapeutic applications.



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sciforum-133467: Phytochemical Profiling, Antioxidant Activity, and Toxicological Assessment of *Abies marocana* Trab. Woody Biomass: Pharmacognostic Evaluation of an Endemic Moroccan Species

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Morocco's botanical wealth includes numerous endemic species with underexplored pharmacological potential. *Abies marocana* Trab., a conifer native to the Rif Mountains, remains insufficiently studied despite its traditional significance. This study aims to evaluate the phytochemical composition, antioxidant activity, and acute oral toxicity of the woody biomass (twigs and cones) of *Abies marocana* Trab., providing insights into its pharmacognostic value.

Proximate composition (moisture, ash, fiber, protein, carbohydrates, and lipids) was determined using AOAC protocols. Mineral elements were quantified via Inductively Coupled Plasma Optical Emission Spectrometry (ICP-OES). Methanolic extracts were analyzed for total phenolics, flavonoids, tannins, and phytosterols, and their antioxidant potential assessed using the DPPH radical scavenging assay. Volatile compounds were identified by Gas Chromatography–Mass Spectrometry (GC-MS). Acute oral toxicity was evaluated in Wistar rats according to OECD guideline 423.

The results revealed that both cones and twigs contain appreciable levels of nutrients and essential minerals. Phytochemical screening confirmed the presence of bioactive secondary metabolites. GC-MS analysis identified linoleic acid as the major compound in twig extracts and 2-Bornanone in cone extracts. The extracts exhibited significant antioxidant capacity, supporting their potential use in oxidative stress-related disorders. Toxicological evaluation showed no signs of toxicity or mortality up to 1000 mg·kg^{−1}, suggesting a favorable safety profile.

These findings highlight the potential of *Abies marocana* Trab. woody biomass as a valuable source of natural antioxidants with prospective applications in phytotherapy, nutraceuticals, and cosmeceuticals. Further pharmacological and mechanistic studies are warranted to support its integration into evidence-based medicinal use.



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sciforum-151603: Polymer-Based Biocomposites Enriched with Glycosaminoglycans for Regenerative Medicine – Synthesis and Characterization

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In this study, innovative polymer-based biocomposites intended for regenerative medicine applications were developed and characterized. The materials were obtained by combining synthetic polymers with natural components such as collagen and gelatin, and further enriched with bioactive additives from the glycosaminoglycan group. The resulting composites exhibited structural and mechanical properties comparable to natural tissues, making them suitable candidates for scaffolds supporting tissue regeneration.

Comprehensive characterization was performed, including analysis of morphology and porosity, stability under conditions mimicking physiological environments, and evaluation of fundamental physicochemical parameters. The average porosity of the materials was $21 \pm 2\%$. The biocomposites exhibited a swelling ratio of 2.8 ± 0.3 g/g after 24 hours of incubation in PBS (pH 7.4), while maintaining structural stability for at least 14 days. During incubation in phosphate-buffered saline, the pH of the medium remained stable in the range of 7.2–7.5, indicating the absence of acidic or alkaline degradation of the material.

The findings indicate that the developed polymer-based biocomposites represent a valuable alternative to conventional biomaterials currently applied in tissue engineering. They provide a promising platform for the advancement of regenerative strategies aimed at the repair and restoration of both soft and hard tissues.

This research was carried out within the SMART-MAT Functional Materials Science Club of the Faculty of Materials Engineering and Physics at Cracow University of Technology (section SmartMat) and as part of the project entitled, „ Polymer Biocomposites for Regenerative Medicine” financed by the FutureLab organization operating at Cracow University of Technology



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sciforum-152079: Preparation of a *Punica granatum* L. peel extract rich in punicalagin and evaluation of its antifungal activity

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Pomegranate (*Punica granatum* L.) is one of the richest fruits in polyphenols, compounds with valuable antioxidant and antimicrobial properties. In recent decades, there has been an ever-increasing demand for its fruits, primarily for juice production, accompanied by a growing generation of agri-food waste, estimated at 9 tons for each ton of pomegranate juice produced.

In this study, the peels of the pomegranates discarded for colour and shape, inappropriate for sale, granted by an Italian farm, were extracted with 95% ethanol. Subsequently, the enrichment of the phenolic compounds in the extract was achieved through solid phase extraction (SPE) by sequential elution with water, water/acetonitrile 1:1 v/v and acetonitrile as mobile phase. The phenol-rich extract was subjected to HPLC-PDA, revealing the presence of high amount of punicalagin (36.1 ± 3.2 %), along with ellagic acid and ellagic acid derivatives.

To evaluate the possible application of the punicalagin-rich extract within formulations for environmental or human/veterinary use, it was tested on six phytopathogenic fungi (from the culture collection of the Fungal Biodiversity Laboratory of Sapienza), reported also as pathogenic for humans or animals, assessing fungistatic and fungicidal activity through the microdilution broth method. MIC and MFC values for the extract and fluconazole, as drug reference, were determined. For four species (FBL number: 4, 57, 59, 659) MIC 90 was observed to be in the range of 500-1000 $\mu\text{g/mL}$, while the respective MFC was 2000 $\mu\text{g/mL}$; however, only three (FBL 4, 57, 659) showed MIC 100 at 1000 or 2000 $\mu\text{g/mL}$. Interestingly, FBL 4 was more sensitive to pomegranate extract than to fluconazole (MIC₉₀ > 64 $\mu\text{g/mL}$).

In conclusion, in this study, the preparation of a pomegranate peel extract rich in compounds with valuable biological activities paves the way for an innovative valorisation of pomegranate waste products, representing an efficient example of circular economy.



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sciforum-151332: Probing the Inhibitory Effects of Barteria nigritana Synthesized Zinc Oxide Nanoparticles Against Alpha Glucosidase Implicated in Diabetes Upsurge

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The escalating global prevalence of diabetes, particularly type 2 diabetes, underscores the urgency of developing novel therapeutic strategies. One such approach is the inhibition of α -glucosidase, an enzyme crucial in the breakdown of carbohydrates, thus influencing postprandial blood glucose levels. This study aimed to investigate the inhibitory effect of *Barteria nigritana* green-synthesized zinc oxide on α -glycosidase, a key enzyme implicated in the progression of diabetes. The phytochemicals present in the compound were determined using standard procedures to achieve this aim. The chemical composition of the synthesized BNZnONPs was characterized using GC-FID analysis. Molecular interaction of all the identified compounds with α -glucosidase was appraised via the Glide XP-docking panel of Schrodinger suite v12.4, while the Adsorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET) prediction of the best-fit compounds was made using the SwissADME search engine. Furthermore, in vitro analysis of the α -glucosidase inhibitory activity of *B. nigritiana* zinc nanoparticles was investigated using a conventional method. The GC-FID screening identified twenty compounds with highest abundance of Catechol, (+)-Pinoresinol, Pyrogallol, Picric acid, Flavanone, 2, Hydroxyl phenol, and Assculetin (50.4, 32.2, 9.3, 7.9, 7.8, and 7.0 ppm respectively) and the compounds with the low concentrations were Resveratrol, Phloroglucinol, Phenetole, Alpha naphthol and 3,4-Hydroxyl toluene (2.4, 2.0, 2.3, 2.2 and 2.2 ppm, respectively). Among the identified compounds, resveratrol, 2-hydroxylphenol, 2, 3-dihydroxylphenol, α -naphthol, and flavonones demonstrated the highest interaction with α -glucosidase, recording docking scores of -7.763, -7.025, -7.018, 6.778, and -6.714 Kcal/mol, respectively. These compounds interacted predominantly with amino acid residues within and around the α -glucosidase active site, using hydrogen bonding. The ADMET properties indicate that 2-hydroxyphenol, 3,4-hydroxyphenol, α -naphthol, and flavonones exhibit favorable drug-likeness, pharmacokinetic properties, and a good safety profile. Interestingly, the nanoparticles demonstrated a very good inhibitory action against α -glucosidase with IC₅₀ values of 4.22 μ g/mL. Thus, *B. nigritina* phytochemicals are promising potential targets for the treatment and development of an anti-diabetic drug.



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sciforum-151737: Soy Lecithin-Based Lipid Nanocarriers for the Delivery of *Cannabis sativa* Extract with Photoprotective Activity

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Vesicles are supramolecular structures formed by self-assembled bilayers of surfactants in aqueous solution. These structures are used as carriers for biologically active molecules delivery, as they can enhance the solubility and bioavailability, and increase cellular uptake of certain drugs. In this study, we evaluated the incorporation of a full-spectrum ethanolic extract of chemotype III *Cannabis sativa* (EECs), containing acid cannabidiol as the main cannabinoid (18%) over tetrahydrocannabinol (1%). Cannabis extracts are known for proven therapeutic and antioxidant properties, although the low water solubility limits its use in aqueous formulations.

Large unilamellar vesicles (LUVs) made from soy lecithin were used as encapsulation systems for the extract. LUVs and EECs-loaded LUVs (EECs-LUVs) were prepared by the extrusion method mixing soy lecithin with different concentrations of EECs (10, 20, 30, 50 µL/mL) in ethanol. Vesicles formation was confirmed by dynamic light scattering, and incorporation of extract components was evidenced by fluorescence spectroscopy.

Photoprotective effect of the encapsulated extract was evaluated using eosin as a model dye. Eosin solutions in the presence and absence of LUVs and EECs-LUVs were irradiated with UV light (254 nm) for 1 to 9 minutes, and eosin degradation was monitored using UV-visible spectroscopy. Results showed a 50–75% reduction in eosin photodegradation in the presence of EECs-LUVs compared to eosin in water or with LUVs.

Also, a preliminary cytotoxicity assessment was carried out by evaluating the hemolytic effect. No significant differences in hemolysis were observed between cells incubated with EECs-LUVs and the control group, up to the highest concentration tested (0.5 mg/mL).

These findings demonstrate that EECs-LUVs are biocompatible and represent a potential carrier for cannabis extract. Moreover, they confirm the photoprotective effect of the encapsulated extract, suggesting applications in the development of new formulations that enhance stability under UV radiation and preserve other sensitive compounds within the matrix.



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sciforum-151493: Unraveling the Antidiabetic and Antidepressant Effects of Crude Methanolic Extracts of *Clitoria ternatea* Flower in Diabetic Mice

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Clitoria ternatea L. (CT) is a perennial herbaceous plant with deep blue flowers native to tropical Asia. Present study aims at characterization of phytochemicals from crude methanolic extract of CT flower and evaluation of antidiabetic and antidepressant effects on 15% fructose induced diabetic mice. GC-MS was employed for identification of chemical constituents from CT flower. Molecular docking and *in-silico* ADMET analysis were performed to validate the results. Thirty-one phytochemicals were identified. In diabetic mice, metformin reduced glucose from 13.82 ± 0.69 to 11.46 ± 1.03 mmol/L after 1 week and 7.68 ± 0.40 mmol/L after 2 weeks. CT extract at 200 and 400 mg lowered glucose to 10 and 6.8 mmol/L after the 1st and 2nd week, respectively. In behavioral test, within 5 minutes, average head-dipping increased from 5.7 ± 1.21 to 11.5 ± 1.64 and for metformin, while it increased to 11.5 ± 1.64 and 13.8 ± 1.83 for 200 mg and 400 mg after 1st week. All three groups reached ~21 dippings after 2nd week. In Tail Suspension Test (TST), immobility time 20.9 ± 1.59 decreased to 13.6 ± 1.12 seconds, 14.8 ± 1.45 seconds, and 8.3 ± 0.59 seconds after 1st week, and to 8.1 ± 1.15 seconds, 8.6 ± 0.79 seconds, and 6.8 ± 1.01 seconds after 2nd week for metformin, 200 mg and 400 mg, respectively. In Elevated Maze Test (EMT), diabetic mice exhibited 5.8 ± 1.33 exploratory movements within 5 minutes, increasing to 14 ± 1.26 , 15 ± 1.26 , and 19.3 ± 1.86 after 1 week, and 14.5 ± 0.55 , 19.5 ± 2.07 , and 23.5 ± 2.26 after 2 weeks for metformin, 200 mg and 400 mg, respectively. Molecular docking studies against five anti-diabetic and five anti-depressant targets further validated the findings, and Stigmasterol and γ -Sitosterol exhibited best results (-7.0 to -10.5 kcal/mol) which also complied with good ADMET profile. Our study connects the outcomes of *in-vivo* and *in-vitro* anti-diabetic and anti-depressant activities to the molecular mechanisms involved in treating diabetes and depression by the drug-like constituents present in CT flower.



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sciforum-152343: Wild Mushrooms as Neuroprotective Reservoirs: Polyamine-Enriched Antioxidant and Anti-Acetylcholinesterase Activities

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This study investigated the mycochemical composition and bioactive potential of three wild mushroom species—*Cortinarius trivialis*, *Mycena pura*, and *M. rosea*—sampled from Tara Mountain, Serbia. The focus was on their polyamine content, total phenolics, total flavonoids, antioxidant capacity (DPPH, ABTS, NO, and FRAP assays), and acetylcholinesterase (AChE) inhibitory activity. Polyamines (PAs) (putrescine, spermidine, spermine) were quantified in lyophilized fungal samples using high-performance liquid chromatography with fluorescence detection (HPLC-FD). In addition, total phenolics, total flavonoids, antioxidant capacity, and anti-AChE activity were determined from 80% methanolic extracts using previously established spectrophotometric methods. Quantification of putrescine (PUT), spermidine (SPD), and spermine (SPM) revealed *C. trivialis* as particularly enriched in PUT (47.51 ± 15.92 mg/kg d.w.) and SPD (41.58 ± 18.06 mg/kg d.w.), while *M. pura* and *M. rosea* contained lower amounts. *M. pura* stood out for its high phenolic and flavonoid content, driving strong antioxidant activity across DPPH, ABTS, FRAP, and NO radical assays. *M. rosea* displayed selective ABTS scavenging and the strongest AChE inhibition ($93.24 \pm 7.90\%$), whereas *C. trivialis*, despite modest antioxidant activity, combined rich polyamine levels with notable AChE inhibition. Principal component analysis underscored distinct metabolic signatures: phenolic-driven antioxidant defense in *M. pura*, SPD-associated neuroprotection in *M. rosea*, and high PUT accumulation in *C. trivialis*.

To the best of our knowledge, this is the first report linking polyamine profiling with AChE inhibition in these mushroom species. The findings highlight a species-specific interplay of polyphenols and polyamines in shaping antioxidant and neuroprotective activities, positioning these inedible fungi as promising reservoirs for bioactive compounds with potential applications in functional foods, nutraceuticals, and neuroprotective strategies.



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Session 6. Novel and Sustainable approaches in Medicinal Chemistry

sciforum-152326: Rational Design and Synthesis of Melanostatin Derivatives to Probe Structural and Functional Diversity

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N-Hydroxy peptides have recently attracted attention for their distinct conformational and physicochemical properties, which markedly influence biological activity. However, incorporating *N*-hydroxyproline into peptide sequences is synthetically demanding, typically requiring complex transformations with several protection/deprotection steps that reduce efficiency and sustainability of the synthesis process. In this study, we present an innovative strategy for the *N*-hydroxylation of proline in peptides using an on-site oxidation strategy via Cope elimination under mild conditions. The methodology is showcased through the assembly of an *N*-hydroxylated derivative of melanostatin neuropeptide.

Our approach demonstrates that the *N*-(cyanoethyl) group serves as a protecting moiety during peptide synthesis and as a leaving group in the oxidation step. Using *N*-(cyanoethyl)-L-proline as the starting material, peptide coupling with H-L-Leu-Gly-OMe afforded a melanostatin intermediate that, upon treatment with *m*-chloroperbenzoic acid, underwent an efficient Cope elimination to introduce the *N*-hydroxy group at the proline residue.

This single-step oxidation under mild conditions delivered the desired tripeptide with excellent yield (93%), avoiding additional deprotection steps. Comparative experiments revealed that incorporating the *N*-(cyanoethyl) group earlier in the synthesis significantly improved the global yield (78%) relative to late-stage derivatization (41%).

Overall, this work presents a novel strategy for the selective modification of prolyl-containing peptides, exemplified by the assembly of *N*-hydroxy-melanostatin. This on-site oxidation methodology, based on Cope elimination, offers a valuable tool for the development of bioactive *N*-hydroxylated peptides.



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sciforum-152149: Catalyst-Free Green Synthetic Approaches for Bioactive Metabolites of *Simarouba glauca*: Toward Sustainable Drug Discovery

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Simarouba glauca, commonly known as the paradise tree, is a tropical medicinal plant rich in bioactive compounds, including quassinoids, triterpenes, flavonoids, and alkaloids, which exhibit notable anticancer, antimalarial, and anti-inflammatory activities. This mini-review critically examines literature from 2010-present to evaluate the chemical composition, pharmacological potential, and sustainable preparation strategies of these metabolites.

A particular focus is placed on **catalyst-free green synthetic approaches**, including solvent-minimized extractions, mechanochemical grinding, microwave-assisted isolations, and photochemical or multicomponent transformations. These methods allow the derivatization or isolation of natural products **without metal catalysts or harsh reagents**, minimizing environmental impact and avoiding residual contamination—key factors in developing clinically viable pharmaceuticals.

In addition, drug-delivery challenges such as poor solubility and limited bioavailability are addressed through literature-reported nano-formulations, liposomal carriers, and polymeric micelles that enhance stability and pharmacokinetic properties. Integrating green synthetic strategies with medicinal-chemistry perspectives highlights the potential of *S. glauca* metabolites as **small-molecule drug candidates** and illustrates a pathway toward environmentally responsible pharmaceutical development.

This literature-based perspective demonstrates how combining **natural-product chemistry, catalyst-free sustainable methodologies, and modern pharmaceuticals** can advance drug discovery while reducing chemical waste. The review underscores key research gaps and proposes future directions for translating the bioactivity of *Simarouba glauca* into safe and sustainable therapeutic applications.



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sciforum-152285: Evaluation of Curcumin and Its Derivatives as Photosensitizers for Antibacterial Photodynamic Therapy through an In-House Irradiation Assay

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Antimicrobial resistance (AMR) poses a critical global health challenge, necessitating the development of alternative, non-antibiotic strategies. Antimicrobial photodynamic therapy (aPDT) represents a promising approach, employing the combined action of a photosensitizer (PS), visible light, and molecular oxygen to generate reactive oxygen species (ROS) that eradicate microbial cells. In this study, we established a standardized irradiation assay and investigated the suitability of curcumin and five structurally related derivatives as candidate PSs for aPDT applications. The compounds were characterized for their optical absorption properties using UV–Vis spectroscopy and subsequently tested for photodynamic antibacterial efficacy against representative Gram-positive and Gram-negative species: *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*. High-throughput growth inhibition assays were conducted under blue light irradiation (470 nm), enabling determination of half-maximal inhibitory concentrations (IC₅₀).

Curcumin displayed broad-spectrum phototoxicity, achieving bacterial growth inhibition with moderate IC₅₀ values. Several derivatives, including monodemethoxycurcumin and analogues with extended conjugation, exhibited distinct absorption shifts and, in selected cases, enhanced antibacterial potency. However, activity patterns varied across bacterial types, reflecting trade-offs between favorable photophysical properties and effective microbial uptake. These findings underscore the importance of structure–activity relationship (SAR) insights in optimizing PS design.

Overall, curcumin remains a safe and accessible scaffold for aPDT, but targeted chemical modifications—particularly those improving aqueous solubility and penetration of Gram-negative outer membranes—are essential to enhance therapeutic potential. This work provides a framework for rational design of next-generation curcumin-based photosensitizers toward clinically viable antimicrobial photodynamic therapies.



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sciforum-152135: Piperidine Derivatives as Next-Generation Dual Cholinesterase Inhibitors: From Rational *In Silico* Design to *In Vitro* Validation.

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Introduction: Alzheimer's disease (AD) necessitates novel therapeutics. This study aimed to design and develop new heterocyclic cholinesterase inhibitors using a rational, integrated computational and experimental approach, with a focus on achieving potency and selectivity, particularly for butyrylcholinesterase (BuChE).

Methods: Novel piperidine-based analogues were designed via molecular docking simulations against acetylcholinesterase (AChE) and BuChE to predict binding modes. Seven designed compounds were synthesized, and their structures were confirmed using TLC, melting point, UV, IR, EI-MS, and ¹H-NMR. In vitro inhibitory activity was evaluated against both enzymes using the Ellman assay, with donepezil as a reference standard. Drug-likeness was assessed based on Lipinski's Rule of Five and blood-brain barrier permeability predictions.

Results: Docking studies elucidated a binding mode involving anchoring in the catalytic site and π - π interactions in the peripheral site. In vitro testing identified two potent dual inhibitors, P8 (IC₅₀ = 11.5 μ M for BuChE) and P14 (IC₅₀ = 15.3 μ M for BuChE), which outperformed donepezil for BuChE inhibition. The series exhibited a selective profile favoring BuChE. Structure-activity relationship (SAR) confirmed terminal group planarity as critical for potency. All compounds exhibited favorable drug-like properties.

Conclusion: The study successfully identifies P8 and P14 as promising, drug-like lead compounds with a superior BuChE-inhibitory profile, making them viable scaffolds for developing next-generation AD therapeutics. The work validates the combined computational and experimental framework for rational inhibitor design



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sciforum-149013: A Novel Hierarchical Support Vector Regression Approach for Predicting BBB Penetration

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Introduction: Blood–brain barrier (BBB) penetration is a crucial factor to assess in central nervous (CNS) system drug development. This criterion is commonly expressed as the unbound brain-to-plasma ratio ($K_{p,uu,brain}$) determined through *in vivo* and *in vitro* methods (e.g., microdialysis, brain slices). Nevertheless, these experimental tests are costly and time-consuming, limiting their application in early drug discovery.

Methods: In this study, we present a novel **hierarchical support vector regression (HSVR)** model to predict $\log K_{p,uu,brain}$ values directly from molecular descriptors. A curated dataset with experimentally measured $K_{p,uu,brain}$ values was utilized to develop and validate the *in silico* models.

Results: The HSVR ensemble model achieved **high predictive performance** with no signs of overfitting across training, test and outlier sets. In addition, it demonstrated robust performance in mock testing with independent datasets, confirming its broad applicability. Importantly, HSVR outperformed commonly used models such as the Brain Penetration Predictor and Brain Exposure Efficiency Score. Beyond quantitative prediction, HSVR also accurately classified BBB⁺ versus BBB[−] compounds and achieved higher **accuracy than SwissADME, lightBBB, and alvaRunner** across multiple $K_{p,uu,brain}$ cut-off thresholds.

Conclusions: Overall, HSVR provides a **robust, interpretable, and cost-effective tool** for predicting BBB penetration. It enables early decision-making, reduces reliance on animal testing, and accelerates the identification of CNS-targeted therapeutics.



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sciforum-151176: Application of Design of Experiment® AQbD Approach for Systematic Optimization of Reverse-Phase High Performance Liquid Chromatography Method to Analyze Simultaneously Two Drugs (Metformin HCl and Sitagliptin) in Tablet Dosage Form

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Abstract: Green analytical techniques aim to replace or minimize the use of hazardous organic modifiers with environmentally friendly solvents without compromising chromatographic performance. This shift enables industries and research laboratories to adopt sustainable analytical methods. Metformin HCl (MF) and Sitagliptin (SITA) are widely used in managing type 2 diabetes mellitus to maintain blood sugar levels in adults when combined with a proper diet and regular exercise. The present study focuses on the Analytical Quality by Design (AQbD)-established development of an easy, quick, precise, accurate, cost-effective, and eco-friendly reversed-phase high-performance liquid chromatography (RP-HPLC) method for concurrent estimation of MF and SITA. A Design of Experiments (DoE) strategy was employed for multivariate optimization of chromatographic conditions, while risk assessment using an Ishikawa diagram helped identify the critical method parameters (CMPs). Factor screening was initially executed by the one-factor-at-a-time (OFAT) approach through trial runs under varying chromatographic conditions. Subsequently, a Box-Behnken Design (BBD) was used to study response surface methodology, enabling detailed evaluation of critical analytical attributes (CAAs)- retention time, resolution, symmetry factor, and peak area as indicators of robustness. Optimization was achieved using a desirability function, yielding mobile phase composition with 25 mM CH₃COONH₄ buffer (pH adjusted to 4.5 using 1 M OPA solution) and ethanol (45:55, v/v) at a flow rate of 1.157 mL/min. Separation was carried out on a HiQ sil C18HS column (4.6 mm I.D. x 250 mm length, 5 µm, 100Å), with the column oven temperature maintained at 25 °C and the detection wavelength at 256 nm. The optimized method was validated according to ICH (Q2R2) guidelines. Overall, the outcomes demonstrate that the AQbD approach effectively facilitates the development and optimization of an eco-friendly RP-HPLC method for the concurrent estimation of MF and SITA in prolonged-release tablets.



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sciforum-151995: Development of New Quality Control Methods for Prospidium Chloride Using the ESI-HPLC-MS System

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Introduction. Research interest in orphan drugs has been growing annually. Consequently, new research studies and developments in quality control for this class of medicinal products are required. Given the relevance of this issue, **the aim of this study** is to investigate the fragmentation mechanism (FM) of the prospidium chloride (PrsCl_2) molecule under electrospray ionization (ESI) to develop new quality control methods using the ESI-HPLC-MS system. **Materials and Methods.** Prospidium chloride substance (PrsCl_2 , $M_r=500.3$). Orbitrap Exploris 120 mass spectrometer, equipped with a Vanquish liquid chromatograph (Thermo Scientific, USA) and an AcclaimTM RSLC 120 C18 analytical column from Dionex Bonded Silica Products (Thermo Scientific, USA). Sample injection volume: $V=5\text{ }\mu\text{L}$; total analysis time: $t=19$ minutes. Studies were conducted with aqueous solutions at a concentration of 0.05 mg/mL . **Results.** The study describes the FM of singly and doubly charged ions formed from the active pharmaceutical ingredient (API): $m/z=445,1819\text{ }[M - \text{Cl}]^+$, $m/z=409,2129\text{ }[M - 2\text{Cl} - \text{H}]^+$, $m/z=205,1101\text{ }[M - 2\text{Cl}]^{2+}$. However, as demonstrated, these ions may originate not only from the API but also from related impurities. This is critical to consider, as the presence of related impurities may overestimate quantitative analysis results. The study also highlights the FM of ions presumably formed from PrsCl_2 derivative compounds: $m/z=373.2365\text{ }[M - 3\text{Cl} - 2\text{H}]^+$, $m/z=187.1219\text{ }[M - 3\text{Cl} - \text{H}]^{2+}$, $m/z=169.1336\text{ }[M - 4\text{Cl} - 2\text{H}]^{2+}$. The study results can contribute to the development of a method for determining the purity of the substance.

Conclusion. The demonstrated FM of the PrsCl_2 molecule and its derivatives during chromatographic-mass spectrometric analysis enables the development of methods for qualitative and quantitative analysis, as well as the determination of the purity of the PrsCl_2 substance.

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sciforum-151564: Evaluating the window of opportunity for intranasal insulin therapy in a rat model of cerebral ischemia

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Intranasal insulin (InI) demonstrates clinical efficacy in mitigating cognitive deficits. Its neuroprotective potential in cerebral ischemia is of growing research interest. For the first time, this study investigates the therapeutic window for InI in a rat model of transient global cerebral ischemia. Cerebral ischemia was induced in male Wistar rats via 10-min bilateral common carotid artery occlusion with hypotension (40 mm Hg) (I/R). Sham-operated (SO) controls underwent surgery without occlusion or hypotension. InI (0.5 IU/rat) was administered at 2 or 4 hours after ischemia, followed by once-daily dosing for 7 days. Hippocampal gene expression and neuronal survival were assessed using RT-PCR and Nissl staining, respectively. InI at 2 h post-ischemia more effectively prevented body weight loss in I/R rats compared to the 4 h regimen. Blood glucose levels remained unchanged across groups. Increased gene expression of GFAP, a marker of astrocytes, and IBA-1, a marker of microglia, was found in the hippocampus of I/R rats, which may indicate astrogliosis and microgliosis. InI, administered at 2 h, normalized the expression of these genes. Moreover, only the 2 h InI treatment group exhibited a significant neuroprotective effect, with a higher density of Nissl-positive neurons in the hippocampal CA1 region compared to untreated I/R rats, consistent with the levels observed in SO animals. This study is the first to define a critical window of opportunity for InI treatment in transient cerebral ischemia. Administration initiated within 2 hours post-ischemia provides neuroprotection and attenuates glial activation, while delayed treatment (4 h) is markedly less effective.

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sciforum-151507: Exogenous Neuraminidase as a Tool to Model LDL Desialylation and Accelerated Atherosclerosis in ApoE-KO Mice

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Introduction: Atherosclerosis remains the leading cause of mortality from cardiovascular diseases. It is driven by lipid accumulation within arterial walls due to retention of low-density lipoproteins (LDL). Among the atherogenic LDL modifications, desialylation – the enzymatic removal of terminal sialic acids from surface glycans – represents a critical but insufficiently studied mechanism. This study aimed to establish a novel in vivo model of sustained LDL desialylation in apolipoprotein E-knockout (ApoE-KO) mice and assess its contribution to atherosclerosis progression.

Methods: *Vibrio cholerae* neuraminidase (Neu) was conjugated to murine IgG using EDAC, purified by affinity batch chromatography, sterilized by filtration and validated by PAGE. Male ApoE-KO maintained on a chow diet received repeated Neu injections for 6 weeks. LDL desialylation was quantified by the thiobarbituric acid assay. LDL atherogenicity was assessed using RAW264.7 macrophages. Morphometric analysis of aortic lesions was performed. Biochemical and hematological parameters were measured to evaluate systemic toxicity.

Results: Neu administration significantly reduced LDL sialic acid content and enhanced cholesterol accumulation in RAW264.7 macrophages incubated with LDL from treated ApoE-KO mice, compared with LDL from wild-type mice. Treated animals exhibited elevated LDL/HDL ratio and LDL cholesterol levels, and a significant enlargement of atherosclerotic lesions. Importantly, Neu treatment did not induce adverse changes in biochemical or hematological parameters, indicating the absence of systemic toxicity.

Conclusions: We developed a novel in vivo model that replicates the enhanced atherogenicity of desialylated LDL and its contribution to atherosclerotic lesion progression. This study provides an experimental platform for studying glycosylation-dependent mechanisms in atherosclerosis and highlight LDL desialylation as a potential therapeutic target.



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sciforum-132286: Exploring Nature's Remedy: The wound-Healing Power of *Inula viscosa* leaf.

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Inula viscosa, which is also known as false yellow head or sticky fleabane, is a flowering plant with powerful potential. Traditionally, this plant was used in phytomedicine due to its significant properties like anti-inflammatory, antiseptic, and antioxidant activities. Consequently, a rotary evaporator was employed to get the aqueous crude extract of this plant, utilizing distilled water as the extraction medium. Total phenolic, flavonoids, and tannin content and DPPH radical scavenging activity were examined to assess the antioxidant ability in the extract. Volatile components found in the *Inula viscosa* essential oil were analyzed with the help of GC-MS after hydro distillation extraction. A cream was prepared containing 5% aqueous crude extract and 2% essential oil from the *Inula viscosa* plant, where these two components have synergetic effects, producing the best results. An incision was made on 9 mice, and they were split into 3 groups: the control group receiving only the cream base on the wound, and the two other groups being administered treatment of Fucidin or *Inula viscosa* cream, respectively. Results showed that the *Inula viscosa* cream significantly aided in diminishing the wound area, achieving closure and appropriate healing in a shorter period without any complications. Hence, *Inula viscosa* cream has proven to have powerful wound healing capabilities.



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sciforum-151735: Meso-methyl-BODIPY conjugate with cabozantinib as a red-light-activated prodrug for anticancer therapy

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Photoactivated chemotherapy is a new strategy for the development of anticancer drugs in which the activity of a chemotherapeutic drug is controlled by light irradiation. This avoids systemic toxicity and reduces side effects. The aim of this work was to evaluate the therapeutic potential of the light-activated prodrug BODIPY-Cab. The tested conjugate consists of cabozantinib, which was used as a cytostatic, and meso-methyl-BODIPY as a photoremovable protecting group (PPG), which is also used as a photosensitizer, allowing for combined therapy.

The photochemical and photophysical properties of the compound were evaluated using a spectrophotometer-spectrofluorometer. To study the biological properties, cell cultures with different expression of target receptors were selected: A-431 (human epidermoid carcinoma), MDA-MB-231 (human breast adenocarcinoma), HEK293 (human embryonic kidney). A laser scanning confocal microscope was used to study the intracellular localization of the BODIPY-Cab. The effect of compounds on cell viability was estimated using the microculture tetrazolium test.

The conjugate has absorption maxima at 368 and 662 nm and a fluorescence maximum at 678 nm. Irradiation of the BODIPY-Cab solution using a red light demonstrated photodegradation of the conjugate and moderate yield of the cabozantinib derivative. Fluorescence quantum yield of BODIPY-Cab was 16%, and the quantum yield of singlet oxygen was 17%. The compound is localized in mitochondria and the endoplasmic reticulum. Activation of the conjugate by light (655–675 nm), increased cytotoxicity, with the generation of ROS, especially superoxide $O_2^{\bullet-}$. Cabozantinib derivative exhibited lower toxicity in cells compared to conjugate, suggesting that the photosensitizer should play a predominant role in initiating cellular damage.

The possibility of controlled release of a cytostatic under the action of red light is shown. The results can be used for further optimization of PPG based on meso-methyl-BODIPY.

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sciforum-129670: Novel Approaches for the Analytical Evaluation of New-Generation VLP-Vaccines

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Introduction. The work is devoted to the development of an analytical approach to determining the concentration of a next generation of VLP-based vaccines using an innovative method based on the kinetics of diffuse reflection (DRf) in optically turbid media. The quality assessment of the latest VLP-based vaccines containing immunological triterpene hydrocarbon adjuvants is of great importance for the effectiveness of immunobiological products. **The aim** is to develop a new analytical approach based on the kinetics of light reflection in an optically heterogeneous medium for the quantitative determination of VLP vaccines. **Materials and Methods.** Sample vaccine (Gam-VLP-Rota) for the prevention of rotavirus infection (160 mg/dose). Solutions (140–360 mg/ml) of bovine serum albumin (BSA, 98%) as the model sample. Squalene adjuvant («oil-in-water» type), phosphate buffer solution (1:1) as the dissolution medium. Laboratory setup for DRf from a rough surface of a heterogeneous solution, consisting of an IR-diode emitter, aimed at a cuvette with a sample, a CC-Device designed to convert an optical image into an electrical signal, and the original Soft (Vidan®) for chemometric processing of the analogue signal. **Results.** The descriptor sd_2 was selected, demonstrating a linear relationship in the coordinates «family of chemometric descriptors (di) – BSA concentration (C, $\mu\text{g/ml}$)». A calibration line ($y = 4,88 \cdot x - 9,83$, $r=0.9998$) was constructed in the coordinates « sd_2 -C, $\mu\text{g/ml}$ ». The DRf measurements of the VLP-Rota vaccine sample were performed under conditions for BSA solutions ($n=9$). The concentration $C_{\text{practical}}$ of the tested vaccine sample was determined, based on the sd_2 obtained value. The method was validated in accordance with ICH Q2 (R1) guidelines, confirming linearity, accuracy (RSD 5%) and repeatability ($n = 9$, $P = 0.95$). The repeatability error (ϵ) was determined to be 9.34%, indicating acceptable intra-assay variation. **Conclusion.** The proposed DRf method confirms its reliability in routine determination of the concentration of new-generation vaccines.



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sciforum-148653: Porphyrin-based polymers for antifungal photodynamic inactivation of *Candida albicans*

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Fungal infections are a growing health concern, associated with high mortality rates, elevated treatment costs, and an increasing number of hospitalized patients. Consequently, novel therapeutic strategies are urgently needed. In this work, two porphyrin-based polymers, PTPPF₁₆-DAB and PZnTPPF₁₆-DAB, were evaluated as photosensitizers for the photodynamic inactivation (PDI) of *Candida albicans*. These polymers are constructed from 5,10,15,20-tetrakis(pentafluorophenyl)porphyrin (TPPF₂₀) or its Zn(II) complex (ZnTPPF₂₀) as porphyrinic units, and *N,N,N',N'*-tetrakis(3-aminopropyl)-1,4-butanediamine (DAB) as a multifunctional crosslinker. Planktonic yeast suspensions (1×10^6 CFU/mL) in PBS were treated with the polymers (2.5 or 5.0 μ M) for 30 min in the dark. Both polymers rapidly bound to yeast cells within 5 min. Complete elimination of planktonic *C. albicans* was achieved at 5.0 μ M after 30 min of irradiation. Experiments with reactive oxygen species scavengers confirmed that singlet molecular oxygen was the main species involved in the photoinactivation process. These polymers were also effective to photoinactivate *C. albicans* pseudohyphae in PBS, producing a concentration and time-dependent effect with both polymers. A complete loss of cell viability was observed when the cultures were treated with 5.0 μ M. The most pronounced inhibitory effects on biofilms occurred when the polymers were incorporated during the proliferation phase. Against 18-h biofilms, PTPPF₁₆-DAB achieved a ~ 2.3 log reduction, whereas PZnTPPF₁₆-DAB was more effective during the adhesion phase, reducing viability by ~ 2 log. These results suggest that the antifungal performance of the polymers varies according to the metabolic activity and structural organization of *C. albicans* biofilms. The results indicate that both porphyrin-based polymers have potential applications as phototherapeutic agents for fungal inactivation under different culture conditions.



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sciforum-151396: Repurposing Aspirin and Simvastatin into a Bioavailable Co-Crystal with Enhanced Anti-Breast Cancer Activity

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The incessant global burden of cancer, particularly breast cancer, drives the urgent need for innovative therapeutic strategies that improve efficacy while reducing the enfeebling side effects of conventional chemotherapy. Drug repurposing, combined with advanced pharmaceutical engineering, presents a promising avenue for rapid clinical translation. This study investigates the anti-cancer potential of a novel pharmaceutical drug-drug co-crystal (DDC) synthesised from Aspirin, a known chemo preventive agent, and Simvastatin, a statin with emerging anti-tumour properties

The co-crystal was successfully synthesised via mechanochemical grinding and thoroughly characterised. Its enhanced aqueous solubility and unique thermal profile confirmed the formation of a new solid-state phase. *In vitro* biological evaluation (with assays like DPPH, H₂O₂ scavenging, NO scavenging, Protein denaturation and HRBC) demonstrated superior free radical scavenging and anti-inflammatory activities compared to the parent drugs alone. Crucially, the co-crystal exhibited potent anti-proliferative effects against MCF-7 breast cancer cells, significantly reducing cell viability and migration and inducing apoptosis. The IC₅₀ values of DDC, Aspirin and Simvastatin alone were scored to be 49.3987, 68.86, 19.49 µg/ml respectively. Mechanistic insights from RT-PCR analysis revealed profound downregulation of key oncogenic markers (BCL-2, COX-2) and upregulation of the pro-apoptotic BAX gene. Furthermore, the co-crystal remained stable and bioavailable under simulated gastrointestinal conditions, supporting its potential for oral administration. Complementary molecular docking studies confirmed strong binding affinities of the parent molecules to the active sites of the target proteins, rationalising the observed biological activity.

These compelling results position the Aspirin-Simvastatin co-crystal as a highly promising candidate for breast cancer therapy. It exemplifies a rational approach to drug development by enhancing the therapeutic profile of existing drugs through crystal engineering, offering a faster and potentially safer route to novel oncology treatments.

Keywords: Drug-Drug Co-crystal, Drug Repurposing, Breast Cancer (MCF-7), Apoptosis, Molecular Docking, Bioavailability, Solid-State Chemistry.



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sciforum-152269: The Emerging Potential of Chalcogen Functionalization in Drug Discovery

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Among Chalcogen elements, sulfur, selenium, and tellurium, occupy a central position in both nature and synthetic chemistry. Their unique electronic structures give rise to diverse bonding patterns and reactivity, making them indispensable in biological systems and highly attractive in molecular design. Sulfur, for example, is a fundamental component of amino acids, cofactors, and signaling molecules, while selenium plays critical roles in antioxidant enzymes and redox regulation. Tellurium, although less common in biology, has recently emerged as a promising element for creating molecules with distinctive pharmacological and physicochemical profiles. These intrinsic properties explain why chalcogen chemistry has become an increasingly powerful tool for medicinal chemists seeking innovative solutions. In this way, incorporating chalcogen elements into organic frameworks has emerged as a versatile approach for generating novel compounds with significant potential in medicine and materials science. This presentation will highlight our recent efforts on the synthesis of selenium-, sulfur- and tellurium-functionalized molecules as a powerful tool in drug discovery. Recent advances in sustainable synthetic methodologies have made the incorporation of chalcogen atoms more accessible, enabling the design of innovative molecular scaffolds with therapeutic relevance. By showcasing representative examples and future perspectives, I aim to illustrate how chalcogen chemistry can expand the medicinal chemist's toolbox and inspire the development of next-generation drugs.



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sciforum-151609: Thermodynamic Framework for Quantifying Drug Precipitation and Solubility in Cyclodextrin-Based Systems

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An original thermodynamic framework has been developed to describe precipitation–dissolution phenomena of drugs in aqueous systems containing cyclodextrins and auxiliary agents. The central innovation is the degree of drug precipitation, derived from new mass balance equations combined with the Law of Mass Action. This parameter quantifies the fraction of drug present in the solid phase and directly indicates solubility limitations under defined conditions. The methodology allows determination of species distributions—including free drug, ionized forms, binary complexes, and ternary complexes—across aqueous and solid phases as functions of pH and composition. Species molar fractions are normalized to the total apparent solubility, ensuring internal consistency. To support visualization, Diagrams of Heterogeneous Chemical Equilibria were introduced, involving three steps: (i) thermodynamic evaluation of solid-phase stability using precipitation degree, (ii) calculation of molar fractions within stability regions, and (iii) assessment of homogeneous systems containing only soluble species by conventional equilibrium methods. Application to ten commercial drugs, including cimetidine, flurbiprofen, indomethacin, and naproxen, confirmed the predictive capacity of the model. By integrating available equilibrium constants, the methodology quantitatively predicts the extent of drug precipitation and reveals synergistic effects in drug–cyclodextrin–auxiliary agent systems. These predictive advantages are particularly relevant for poorly soluble pharmaceuticals, as the framework identifies conditions where solubility is maximized and precipitation minimized. Overall, the proposed methodology provides both quantitative and graphical tools for analyzing phase behavior, solubility dynamics, and cooperative effects in drug formulations. Beyond pharmaceuticals, the framework has potential applications in environmental and materials science where heterogeneous equilibrium processes of poorly soluble compounds are critical.



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Session 7. Emerging technologies in drug discovery

sciforum-148437: Advanced Technologies of the Two-Dimensional Diffuse Reflection Method in Pharmaceutical Quality Control

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In the current context of viral variability driven by their high mutability, comprehensive measures for prevention, control, and treatment with effective antiviral agents are required, along with the development of rapid and reliable methods for quality control. This work is based on an approach employing the kinetics of diffuse light reflection (DLR) from a rough surface, followed by chemometric processing of dynamic speckle patterns. To this end, mathematical descriptors analogous to QSAR models were incorporated into the calculation algorithm: Wiener (W) and Balaban (J) indices in the Trinaystich modification— d_1 , d_2 , d_3 —as well as two triads of root-mean-square deviations sd_1 , sd_2 , sd_3 ; r_1 , r_2 , r_3 (where $r_i = d_i/sd_i$) and . **The aim** of the study was to develop and validate an analytical method based on 2D-DLR for the quantitative assessment of antiviral drug substances. **Materials and Methods.** Ribavirin (manufacturer Jiangling Benda Pharmaceutical Co., China) – a synthetic nucleoside analog with prominent antiviral activity and antimetabolic properties; model aqueous solutions (concentrations ranging from 0.25 mg/mL to 5 mg/mL, $n=6$; proprietary software (Vidan®). **Results.** A family of 10 descriptors, represented as sequential horizontal bands on the 2D diagram (with d_i corresponding to concentration, $\mu\text{g/mL}$), demonstrated stability of values for a specific sample within intra-laboratory reproducibility, and differentiation among samples with different solution dilutions. Particularly illustrative and statistically significant was the result for the topological descriptor R (correlation coefficient $r=0.9998$). This enabled the construction of a calibration curve in the coordinates “R-concentration ($\mu\text{g/mL}$),” based on the linear equation $y=170.4+55.7 \cdot x$, with $r=0.982$. The method was validated according to ICH Q2 (R1) guidelines, confirming linearity, accuracy (RSD = 7.19%), and repeatability ($n=6$, $P=0.95$). The repeatability error ($\epsilon\epsilon$) was determined to be 7.55%, indicating acceptable analytical variability. **Conclusion.** The 2D-DLR method demonstrated reliability for systematic quantification of concentration of the antiviral ribavirin in aqueous solutions.



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sciforum-152381: Combined effect of oxacillin and photodynamic inactivation on Methicillin-Resistant *Staphylococcus aureus*

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Introduction: Antimicrobial resistance is a high healthiness problem due to constant limitation of their treatment. Methicillin resistance in *Staphylococcus aureus* strains is alarming, due to their unresponsiveness to other β -lactams. With the rise of antimicrobial resistance, Photodynamic Inactivation emerges as alternative in concomitant treatment of infections. Photodynamic inactivation technique uses light to activate photosensitizers, which, when irradiated, generate reactive oxygen species, leading to cell death and cytoskeletal disruption.

Methodology: Zincoporphyrin, ZnP, (ZnTE-2-PyP⁴⁺) was used as a photosensitizer (final concentration 4 $\mu\text{mol}\cdot\text{L}^{-1}$), and oxacillin at concentrations of 8 $\text{mg}\cdot\text{L}^{-1}$, 4 $\text{mg}\cdot\text{L}^{-1}$, 2 $\text{mg}\cdot\text{L}^{-1}$, 1 $\text{mg}\cdot\text{L}^{-1}$, and 0.5 $\text{mg}\cdot\text{L}^{-1}$ in Mueller-Hinton Broth. Strain of *Staphylococcus aureus* MRSA was grown on Mueller-Hinton Agar at $35 \pm 1^\circ\text{C}$ for 24 h, with preparation of suspensions in Saline solution (0.9% w/w) adjusted to optical density (OD) of 0.1 at 625 nm, corresponding to $1.0\cdot 10^8$ cells $\cdot\text{mL}^{-1}$ with final working solution of 106 cells $\cdot\text{mL}^{-1}$. Equals aliquots of ZnP and previous solution were mixed and irradiated for 3 min (6.26 J $\cdot\text{cm}^{-2}$) under blue light, with subsequent exposure of MRSA+ZnP to oxacillin concentrations and incubated at same conditions, with subsequent visual reading to determine the Minimum Inhibitory Concentration. Control conditions in absence of light were performed to ensure the reliability of the tests.

Results and discussion: The light-treated systems showed a reduction in minimum inhibitory concentration on oxacillin from 8 $\text{mg}\cdot\text{L}^{-1}$ to 0.5 $\text{mg}\cdot\text{L}^{-1}$. The systems not exposed to light continued to show oxacillin resistance. The momentary susceptibility to oxacillin in the light-treated group may be due to damage to the bacterial cell wall caused by the photodynamic treatment.

Conclusion: It was observed that concomitant treatment of IFD and oxacillin presents a positive in vitro perspective for infections caused by *Staphylococcus* MRSA, playing an important role in antimicrobial resistance.



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sciforum-151052: Development of a cell-based platform for expression of antimicrobial peptides: modification of HEK-293T cells for expression and extracellular secretion of human β -defensin 1

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Introduction: Antibiotic resistance is recognized as a major public health threat. Antimicrobial peptides provide an alternative to antibiotics. Human β -defensin 1 (hBD1), produced by epithelial cells, demonstrates broad antimicrobial activity and retains stability after proteolysis. However, its clinical application is constrained by high synthesis costs. This study aimed to generate a eukaryotic cell platform for hBD1 expression and secretion.

Methods: Plasmids pHBD1-Out and pHBD1RFP-Out were designed using the pcDNA3.1(+) vector with the CMV promoter. Cloning was performed in *E. coli* XL1-Blue, followed by plasmid purification and restriction analysis. HEK-293T cells were transfected via lipofection. Transfection efficiency was evaluated after 48 h by fluorescence microscopy. hBD1 production was confirmed by PAGE and HPLC. Antimicrobial activity was assessed against *E. coli* using agar diffusion assay.

Results: The pHBD1-Out plasmid carried the hBD1 sequence and the SRP9 signal peptide for extracellular expression, while pHBD1RFP-Out additionally contained A2P peptide and RFP marker. Transfection was confirmed by the presence of fluorescent cells, although the efficiency was relatively low. hBD1 production was detected in both cell lysates and supernatants, showing similar expression patterns for pHBD1-Out and pHBD1RFP-Out. Lysates demonstrated pronounced antimicrobial activity comparable to ampicillin. Supernatants also inhibited *E. coli* growth, though less effectively.

Conclusions: The constructed plasmids enabled efficient hBD1 expression in HEK-293T cells. The recombinant peptide exhibited antimicrobial activity comparable to conventional antibiotics, highlighting the potential of cell-based systems for AMP production and the development of novel antimicrobial therapeutics. This work was supported by the Ministry of Science and Higher Education of the Russian Federation in 2025 (No. 0088-2025-0004).



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sciforum-151590: HDAC4 PROTACs as a potential palliative care therapy for Spinal Muscular Atrophy: Impact of the various linkers on enzymatic activity

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HDAC4 is a class IIa member of histone deacetylases (HDACs), playing a role in regulating gene expression through chromatin remodeling, as well as in muscle alterations. It triggers the atrogin-1 and MuRF1 upregulation, muscle protein degradation, and slow atrophy progression, symptoms associated with Spinal Muscular Atrophy (SMA), for which it is considered an important target for corresponding palliative care therapeutic development.

In that sense, our interests were to develop selective PROTAC degraders of HDAC4 using known co-crystallized HDAC4 inhibitors (HDAC4Is) available at Protein Data Bank as starting points, particularly the truncated version of 6FYZ HDAC4I as a warhead stripped of the Cap moiety, as instructed by the generated preliminary Py-CoMFA 3-D QSAR model. The primary objective during the initial profiling phase was to investigate their interactions with HDAC4 and assess how structural modifications influence potency. To that, the PROTACs were initially autonomously designed by means of Python's RDKit by merging the warhead with the *in-house* available linkers and either VHL-1 or CRBN E3 ligase ligands, respecting the desirable PK/PD profiles. Selected hits were promptly synthesized and submitted to enzymatic fluorogenic assaying, of which TG-49 and PJ594, as VHL-1-related PROTACs, showed remarkable IC₅₀s of 50 and 150 nM. Regarding the whole panel, interestingly, even minor changes in the linker structure resulted in significant variations in the inhibition of HDAC4, suggesting that the linker may play a critical role in mediating interactions with HDAC4. Yet, confirmation is pending with further ternary complex computational modeling and HDAC4 cellular degradation assays.



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sciforum-149014: Machine Learning Based classification Analysis of hERG Blockers for Prevention of Cardiac Toxicity

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The human ether-a-go-go-related gene (hERG) predominantly expresses in cardiac tissues causes long QT syndrome and blockade of this gene leads to cardiotoxicity. Medicinal chemists are working towards for discovering bioactive molecules without hERG blockage. Hence, many strategies have been implemented in last few decades including computational techniques for the design of novel molecules and the machine learning based classification analysis is predominantly used nowadays. In this investigation, 451 compounds with hERG blocking activity (experimental $-\text{LogIC}_{50}$), obtained from literature were considered in the study. For this analysis, the Decision Tree, Random Forest and Random Tree algorithms of WEKA software were applied. The results obtained from the analysis showed that the models developed with complete training set and validated by test set (30%) and 10-fold cross-validation methods provided significant statistical parameters. The contributed descriptors explained that the hERG blockers contain aromatic rings, such as phenyl (C_6H_5) or benzyl ($\text{C}_6\text{H}_5\text{CH}_2$) groups, which can participate in π - π interactions with aromatic residues in the channel. Basic nitrogen atoms, often found in primary ($\text{R}-\text{NH}_2$), secondary (R_2-NH), or tertiary (R_3-N) amines, are common in hERG blockers. Hydrophobic groups, such as alkyl chains (e.g., CH_3 , C_2H_5) or cycloalkyl groups (e.g., cyclohexyl, C_6H_{11}), play a significant role by enhancing binding affinity to the hydrophobic pocket of the hERG channel. The presence of flexible linkers, such as ethylene ($-\text{CH}_2-\text{CH}_2-$) or propylene ($-\text{CH}_2-\text{CH}_2-\text{CH}_2-$) chains, between hydrophobic and hydrophilic parts of a molecule can facilitate optimal orientation within the binding site. Additionally, hydrogen bond donors ($-\text{OH}$, $-\text{NH}_2$) and acceptors (e.g., $-\text{CO}$, $-\text{CN}$) contribute to the binding affinity and specificity of a compound for the hERG channel, although they are less critical than hydrophobic and ionic interactions. This analysis provides information on the physicochemical properties required for the avoiding hERG blockade.



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sciforum-152062: Molecular Profiling Of Breast Cancer: Advancing Biomarkers Discovery And Targeted Treatment Strategies

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Breast cancer remains one of the most significant health risks throughout the world, demanding precise methods for early detection, therapeutic intervention and disease progression monitoring. Despite improving screening and therapy, patient outcomes are highly variable because of complex biology of the disease and therefore validated biological targets and biomarkers are required. Breast cancer heterogeneous disease shaped by genetic, molecular and environmental variables and biomarkers playing a central role in customizing personalized treatment. traditional markers such as hormone receptor (ER, PR) and HER2 status have been applied in clinical decision making but ne research suggests that other molecular signals, circulating tumor cells and microRNAs are promising indicators of tumor behavior and therapeutic response. In this research, tumor tissue and liquid biopsy have been compared using molecular profiling methods and bioinformatics-driven discovery of biomarkers. Immunohistochemistry, PCR-based assays and proteomic techniques have been applied for the identification and validation of novel biomarker panels for specific subtypes of breast cancer. Key findings imply that novel biomarker candidates not only distinguish between aggressive and indolent tumor forms but also predict responsiveness to targeted therapies more accurately over conventional markers. Importantly, integrating these markers in clinical models improved diagnostic specificity and indicated new therapeutic targets for drug development. Identification and validation of new biological targets and biomarkers are the prime innovation of personalized medicine in breast cancer. This research points towards precision oncology's potential to enhance survival and quality of life for patients, offering hope for more effective, individualized treatment regimens in the future.



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Session 8. Radiopharmaceuticals

Session 9. Drug disposition and drug formulation

sciforum-151136: From Leaf to Relief: Bioactive polymeric hydrogel films loaded with *Psidium Guajava* for wound healing potential.

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According to the World Health Organization (WHO), more than 300,000 people die each year as a result of skin injuries, wounds, cuts or burns and auto immune diseases. Wound healing process is a complex biological process which involves several overlapping phases, hemostasis, inflammation, proliferation and remodeling. Inflammation is the major phase of healing process which plays a crucial role for the startup of repairing process. Untreated wound care can lead to prolonged inflammation and complications. Already available skin dressings are dry in nature. These ordinary dressings do not maintain moisture at wound site and also does not deal with optimal wound healing process. Consequently microbial growth leads to pain in patients. In order to lessen side effects associated with ordinary dressings, transdermal hydrogel films of *Moringa oleifera* gum (2%) using *Psidium Guajava* extract (0-4 %) with 0.5% w/v calcium chloride as crosslinking agent were developed by solvent casting method through ionic interaction. First of all gum solution was prepared and dissolved in Polyethylene glycol as plasticizer. Afterwards extract solution was added dropwise and stirred for 15 minutes. Lastly solution was casted in petri dishes and allowed to dry. Higher swelling (%) was observed with formulation having 3 % of guava extract. Physicochemical properties and wound contraction studies were performed on hydrogel films having high mechanical strength and swelling index. The antibacterial activity against staphylococcus aureus causes an inhibition zone ($2.9 \text{ mm} \pm 0.004$) to form around the hydrogel films. No interaction among polymers and uniform surface morphology which support controlled drug release was observed with FTIR and SEM. *In vivo* wound healing studies on rats showed 85 % w/w of percentage wound contraction to treat wound within 10 days. Fabricated polymeric hydrogel films were effective bioactive wound dressings due to their significant anti-bacterial activity, high biocompatibility and wound healing efficacy.



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sciforum-151942: Polymer-Based Solid Dispersions to Improve the Solubility and Dissolution Rate of Ziprasidone Hydrochloride

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Ziprasidone Hydrochloride is an atypical antipsychotic drug commonly prescribed for the treatment of schizophrenia. Its clinical efficacy is significantly limited by its very low aqueous solubility (0.1 mg/mL), which restricts oral absorption and systemic bioavailability. In the present study, we aimed to enhance the solubility and dissolution rate of Ziprasidone Hydrochloride through the formulation of solid dispersions using hydrophilic polymers, including polyethylene glycol 6000 (PEG6000), polyvinylpyrrolidone (PVP), hydroxypropyl methylcellulose (HPMC), and hydroxypropyl cellulose (HPC). Solid dispersions were prepared by the solvent evaporation technique in various drug-to-polymer ratios and subjected to comprehensive physicochemical characterization. The formulations were analyzed using Scanning Electron Microscopy (SEM), Fourier Transform Infrared Spectroscopy (FTIR), Differential Scanning Calorimetry (DSC), and X-Ray Diffraction (XRD) studies. The results revealed that incorporation of Ziprasidone into polymer matrices led to a reduction in particle aggregation, conversion from crystalline to amorphous form, and improved wettability and dispersibility. Optimized solid dispersions exhibited approximately a 50% increase in solubility compared to the pure drug. Dissolution studies demonstrated a significant improvement in release profiles, with drug release directly proportional to the polymer concentration. Among the polymers tested, PVP was the most effective in enhancing solubility and dissolution. These findings indicate that polymer-based solid dispersions are a promising strategy for improving the oral bioavailability and therapeutic efficacy of poorly water-soluble drugs like Ziprasidone Hydrochloride.



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sciforum-150023: Preventing Sepsis by Preemptive Restoration of “Leaky Gut” with an Advanced Probiotic Platform

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Background/Objectives: Sepsis remains a leading cause of global mortality despite advances in critical care, largely because treatment is initiated only after systemic inflammation and organ damage are already established. Emerging evidence highlights gut microbiota dysbiosis and intestinal barrier impairment as critical drivers of sepsis pathogenesis, particularly in immunocompromised patients. We propose that early modulation of the gut microbiome represents a viable prophylactic strategy against sepsis.

Methods: In this study, we designed and fabricated an advanced probiotic delivery platform based on ternary hydrogel microspheres, designated EcN+Muc@SHM. These microspheres were constructed by first encapsulating *E. coli* Nissle 1917 (EcN) and mucin within a methacrylated hyaluronic acid (HAMA) core via a photopolymerization-coupled emulsification method. Subsequently, a protective alginate shell was coated onto the surface through ion polymerization to enhance stability and targeted delivery.

Results: *In vitro* assessments demonstrated the potent bioactivity of the hydrogel components, wherein HAMA and mucin synergistically promoted intestinal cell proliferation, mitigated lipopolysaccharide (LPS)-induced mucus secretion injury in HT29-MTX cells, and alleviated inflammatory responses and oxidative stress in macrophages. Critically, the integrated EcN+Muc@SHM microsphere structure conferred robust protection to the probiotic EcN payload against the harsh gastric environment, as validated both *in vitro* and *in vivo*. In a clinically relevant cecal ligation and puncture (CLP) mouse model, this advanced probiotic platform exhibited remarkable prophylactic and therapeutic efficacy. Administration of the microspheres significantly reduced bacterial translocation, resolved local inflammation, and alleviated intestinal injury. Fecal microbiome sequencing further elucidated the underlying mechanism, revealing that the treatment effectively corrected post-CLP dysbiosis, thereby restoring microbial homeostasis and promoting the recovery of a healthy gut flora.

Conclusions: Our findings underscore the potential of proactive, microbiome-targeted strategies to disrupt the vicious cycle of dysbiosis and inflammation, offering a promising avenue for sepsis prevention in high-risk populations.



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Session 10. Nanomedicine and Nanotechnology

sciforum-150802: Artificial Cell-Derived Vesicles from Ginsenoside Rg1-Primed Mesenchymal Stromal Cells Mitigate Oxidative Stress and DNA Damage in Myocardial Ischemic/Reperfusion Injury

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Myocardial ischemia/reperfusion injury (MI/RI) remains a major challenge in the treatment of acute myocardial infarction due to the lack of effective therapeutic options. Despite advancements in interventional techniques like percutaneous coronary intervention, MI/RI-induced oxidative stress, inflammatory responses, and cardiomyocyte apoptosis still lead to poor long-term prognosis for patients. While mesenchymal stromal cells (MSCs) and their derivatives show promising potential for MI/RI therapy, their clinical application is hindered by low transplantation efficiency—often resulting from poor cell retention in the ischemic myocardium—and insufficient yield for large-scale clinical use. In this study, we engineered nanoscale artificial cell-derived vesicles (ACDVs) by extruding Ginsenoside Rg1-primed MSCs (Rg1-MSCs), resulting in Rg1-ACDVs. Rg1-ACDVs displayed superior therapeutic efficacy compared to non-primed ACDVs and extracellular vesicles derived from Rg1-MSCs (Rg1-EVs), as evidenced by reduced myocardial infarct size in rat MI/RI models. Multi-omics analysis revealed that Rg1-ACDVs possess distinct molecular signatures associated with promoting cell cycle progression and reducing DNA damage, including upregulated expression of DNA repair-related proteins and cell cycle regulators. These findings were further validated experimentally, demonstrating that Rg1-ACDVs effectively reduce reactive oxygen species (ROS) accumulation—an important driver of MI/RI—and mitigate DNA damage both in vitro (in cultured cardiomyocytes) and in vivo (in rat MI/RI models). This study highlights the synergistic benefits of combining Ginsenoside Rg1 priming (which modulates MSC paracrine function) with nanoscale engineering (which optimizes vesicle delivery), and introduces Rg1-ACDVs as a scalable and innovative strategy, offering a promising approach for improving clinical outcomes in MI/RI therapy.



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sciforum-152376: Can polymers influence antifungal activity of silver nanospheres? A study on *Candida albicans*

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Introduction: Silver nanoparticles are well known for their antibacterial, antiviral, and antifungal properties. Although the exact mechanism is not fully understood, it is believed to be strongly related to the release of Ag⁺ ions, which contribute to cell death. Polymers can interact with the cell surface, potentially enhancing ion release and increasing the antimicrobial effect. In this study, we used biocompatible polymers in a seed-mediated growth method to produce silver nanospheres and evaluate their activity against *Candida albicans*. **Methodology:** *Candida albicans* was cultured on Sabouraud Agar and standardized to 10⁶ CFU/mL. Silver nanospheres were synthesized using Carbopol® 940 (CBP), Alginate (Alg), and Sodium Poly-4-Styrene-Sulfonate (PSS), then purified by centrifugation prior to use in the experiments. The nanospheres were incubated with fungal cells for 24 hours. After incubation, each test sample was serially diluted from 10⁻¹ to 10⁻⁴, and 10 µL of each dilution was plated on Sabouraud Agar. **Results and discussion:** Our findings showed that AgNP-PSS resulted in the greatest reduction in fungal activity, with a 4 Log₁₀ reduction, compared to AgNP-CBP (2.7 Log₁₀) and AgNP-Alg (1.7 Log₁₀). We believe this enhanced effect may be related to the presence of sulfur groups in the PSS molecules. **Conclusion:** AgNPs exhibited the expected antifungal activity against *Candida albicans* in vitro, and the results with PSS suggest that polymer interactions play a key role in mediating their mechanism of action.



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sciforum-136318: Phyto-Based Nanocosmetics: A Synergistic Approach to Skincare Innovation

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The cosmetics industry is undergoing a significant transformation, driven by the escalating demand for naturally derived ingredients and advanced delivery systems. This abstract explores the exciting convergence of plant-based bioactives and cutting-edge nanotechnology in developing next-generation cosmeceuticals. We delve into how nanocosmetics, leveraging diverse nanocarriers like niosomes, nanofibers, and nanoemulgels, revolutionize the efficacy and targeted delivery of active compounds. This approach moves beyond mere aesthetics, aiming to offer genuine therapeutic benefits for skin health by enhancing ingredient stability, solubility, and controlled release. These nano-formulations precisely encapsulate and direct beneficial molecules to specific skin layers, optimizing therapeutic impact while minimizing potential side effects.

Our research directly contributes to this paradigm shift. We employ a rigorous, multi-faceted approach, integrating in vitro enzyme inhibition assays, sophisticated in silico molecular docking and toxicity assessments, and comprehensive cell-based studies to pinpoint high-potential plant extracts and natural compounds. This meticulous screening has led to several successful laboratory-scale formulations. For instance, we have successfully incorporated *Cotinus coggygria* extracts into innovative niosome, nanofiber, and nanoemulgel systems, demonstrating enhanced skin delivery and biological activity. Furthermore, our team has developed a patent-pending anti-acne formulation based on a unique blend of plant extracts specifically targeting *Propionibacterium acnes*. We also highlight the broader potential of these nanoforms beyond cosmetics, as shown by our recent development of polycaprolactone (PCL) electrospun nanofibers loaded with *Cotinus coggygria* extract and hyaluronic acid (HA) for advanced wound healing applications. This talk will showcase our latest breakthroughs in crafting these innovative, phyto-based nanocosmeceuticals.



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sciforum-150695: Biomarker-Guided Nanopharmaceutics for Preventing Space-Induced Bone Loss

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Abstract

Spaceflight-associated bone loss poses a major health risk during long-duration missions due to microgravity, altered calcium metabolism, and increased bone resorption. Current countermeasures, including bisphosphonates and exercise, are only partially effective. This seminar explores the concept of biomarker-guided nanopharmaceutics, where bone turnover biomarkers such as C-terminal telopeptide (CTX), alkaline phosphatase (ALP), or osteocalcin serve as triggers for localized and controlled drug release. Smart nano carriers engineered with stimuli-responsive chemistries can deliver anti-resorptive or anabolic agents directly to bone tissue, improving efficacy and reducing systemic side effects. This approach integrates chemistry, pharmaceutics, and nanomedicine to address a critical challenge in space healthcare.

Introduction

Astronauts lose ~1–2% of bone mass per month in microgravity. Traditional pharmacological interventions require frequent dosing and risk systemic toxicity. Biomarker-based pharmaceutics provide precision by linking drug release to biological signals of bone remodeling.

Aim

To design smart nanomedicines guided by bone turnover biomarkers for targeted, on-demand therapy.

Methods

Biomarker Identification: Monitor CTX, ALP, osteocalcin as indicators of resorption/formation. **Nanocarrier Design:** Polymeric/lipid nanoparticles functionalized with bone-targeting ligands (e.g., bisphosphonate moieties). **Stimuli-Responsiveness:** Incorporation of redox- or enzyme-sensitive linkers activated by elevated biomarker levels. **Validation:** *In vitro*: Bone cell culture under simulated microgravity. *In vivo*: Rodent models exposed to hindlimb unloading.

Results

Targeted release of antiresorptives at high CTX levels. Enhanced bone density preservation with lower systemic drug exposure. Adaptive, personalized dosing guided by biomarker fluctuations.

Conclusion

Biomarker-guided nano pharmaceutics represent an innovative pharmaceutical strategy for preventing bone loss in space. By merging biomarker science with smart nano medicine, this approach promises safer, more effective, and adaptive therapies—essential not only for astronauts but also for osteoporosis management on Earth.



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sciforum-150703: Cefazolin-loaded Solid Lipid Microparticles: A novel approach for ocular therapeutics

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Introduction

Eye infections present major challenges for treatment, due to the microbial species and the low ocular bioavailability of drug. A fortified eye drop is, in some case, the only option for administering antibiotics such as Cefazolin. It is an extemporaneous preparation with limit stability and needs to be injected via the painful intraocular route. In order to improve ocular tolerance and the efficacy of Cefazolin, we developed a colloidal eye drop containing lipid microparticles loaded with this drug which can be administrable by instillation.

Methods

Cefazolin lipid microparticles were prepared by high shear homogenization method using an Ultraturrax at 20,000 rpm for 5 minutes. The lipid matrix was composed of carnauba wax and a pair of surfactants. The particle size was evaluated by optical microscopy, while encapsulation efficiency was performed by spectrophotometry at 272nm in water. The *in vitro* release study was conducted in dialysis bag immersed in artificial tear fluid. Microbiological efficacy was assessed on sensitive strains of *Pseudomonas aeruginosa* and *Escherichia coli*. Ocular tolerability was assessed by a HET CAM test on embryonated test.

Results

The lipid microparticles exhibited a monodisperse distribution with a mean diameter of 1.1 μm . The recorded encapsulation efficiency was 87% and the antimicrobial activity was satisfactory. The *in vitro* release of the colloidal eye drop demonstrated enhanced diffusion and a delayed release profile, with a Cmax shift of 50 minutes compared to the aqueous solution of cefazolin. The pH and osmolarity were favorable for ocular administration. The HETCAM results didn't show any sign of irritation at 5 min.

Conclusion

The colloidal eye drop of lipid microparticles encapsulating Cefazolin represents a promising advance in the treatment of eye infections, aiming to enhance intraocular permeability and prolong the action of the antibiotic.



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sciforum-148806: Clindamycin-loaded cinnamaldehyde-based nanostructured-lipid carriers: A potential platform to treat MRSA skin infection

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MRSA skin infection remains a serious health concern. Clindamycin, an FDA-approved lincosamide antibiotic, treats MRSA but is limited topically by the stratum corneum (SC) as a skin barrier. This study developed nanostructured lipid carrier (NLC) to improve clindamycin's efficacy against MRSA wound infections. NLC was prepared using a cold microemulsion technique, optimized, and characterized for its physicochemical properties, with safety confirmed by an MTT assay in HaCat cells. Cinnamaldehyde was selected as the NLC's oily phase due to its antibacterial properties, providing synergistic effects. The clindamycin-loaded cinnamaldehyde-based NLC exhibited a nanometric size of 100.3 ± 3.8 nm, a narrow size distribution (PDI 0.19 ± 0.0002), and a spherical morphology. In vitro antimicrobial activity was assessed on MRSA strains using minimum inhibitory concentration (MIC), minimum bactericidal concentration (MBC), biofilm inhibition, and regrowth bioassays. The loaded NLC enhanced antimicrobial activity against MRSA, showing 2- to 8-fold improvement over free clindamycin and unloaded blank NLC. MIC/MBC values were $1/4$ $\mu\text{g/mL}$ for the loaded NLC, $2/8$ $\mu\text{g/mL}$ for free clindamycin, and $8/64$ $\mu\text{g/mL}$ for blank NLC. At half the MIC concentration, the NLC inhibited MRSA biofilm formation by 67.58%, compared to 48.47% for free clindamycin. Skin permeation through SC was evaluated using Franz cells and showed improved drug permeation of the NLC formulation compared to the free drug. In vivo studies used Albino Wistar rats divided into five groups: uninfected, infected, untreated, infected treated with a marketed drug, infected treated with an unloaded formulation, and infected treated with a loaded NLC. After 7 days, agar cultures showed extensive bacterial growth in untreated rats, minimal growth in rats treated with unloaded formulation, and no growth in the loaded NLC group. Wound diameter measurements confirmed improved healing with the NLC, as analyzed using SPSS version 25. This formulation is a promising antibacterial vehicle against MRSA infections.



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sciforum-151460: Comparative Evaluation of Transethosomal and Transniosomal Emulgels for Enhanced Transdermal Delivery of Naproxen: A Novel Approach for Managing Musculoskeletal Inflammation

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Naproxen, a widely used non-steroidal anti-inflammatory drug (NSAID), is effective in managing musculoskeletal inflammation but is often associated with gastrointestinal side effects and hepatic first-pass metabolism when administered orally. To address these limitations, this study focused on developing and comparing two advanced vesicular drug delivery systems “Transethosomes and Transniosomes” incorporated into emulgels for transdermal delivery of Naproxen. These vesicular systems enhance skin permeation and offer fast release, making them promising candidates for topical NSAID delivery.

A 2-factor, 3-level experimental design was employed to optimize formulation parameters. Naproxen-loaded Transethosomes and Transniosomes were prepared using the thin-film hydration method and subsequently incorporated into hydroxypropyl methylcellulose (HPMC)-based emulgels. The resulting emulgels were evaluated for pH, viscosity, spreadability, FTIR interactions, and in vitro drug release behavior. Optimized formulations, designated TE7 and TN1, exhibited high entrapment efficiency, appropriate vesicle sizes, and desirable physical characteristics. FTIR analysis confirmed compatibility between Naproxen and formulation excipients.

In vitro drug release studies demonstrated efficient Naproxen release, with the Transethosomal formulation (TE7) showing a slightly faster release profile compared to the Transniosomal formulation (TN1). These findings suggest that both emulgel systems offer promising potential as effective transdermal alternatives to conventional oral NSAID therapy for musculoskeletal conditions, potentially improving patient compliance and minimizing systemic side effects.



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sciforum-151365: Design of Gadolinium or Iron based contrast agents for senile plaques detection by MRI

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Introduction: Senile plaques (SP), composed mainly of β -amyloid (β A) peptide fibers, are a distinctive feature of Alzheimer's disease (AD). Visualizing SP using magnetic resonance imaging (MRI) poses a challenge. MRI requires specific contrast agents (CAs) to recognize SP, thereby increasing detection sensitivity. This paper describes the synthesis of two types of CAs: positive or T1 (gadolinium oxide nanoparticles (Gd_2O_3 NPs) or metal complexes supported on silica nanoparticles (SiO_2 NPs)) and negative or T2 (iron oxide nanoparticles (IONPs)). These CAs are functionalized with Amylovis compounds as target ligands (TLs) related to β A in order to design smart probes for the specific diagnosis of AD using MRI. **Method:** Gd_2O_3 NPs, SiO_2 NPs and IONPs were obtained by polyol solvothermal, sol-gel and thermal decomposition methods, respectively. For Gd_2O_3 NPs some experimental conditions were optimized (molar ratio of precursors, solvent, and reaction time). After the functionalization with carboxyl or amino terminal groups, Amylovis compound was grafted to the SiO_2 NPs and IONPs using carbodiimidation reaction. The grafting percentage was indirectly determined by means of the quantification of free Amylovis (HPLC). **Results:** Optimal conditions for the synthesis of Gd_2O_3 NPs were 1:3 as precursor molar ratio, ethylenglycol as solvent and 4 h at 180 °C. All NPs were characterized using FT-IR (evidenced the metal-oxygen bonds and ligands at the surface of NPs), microscopic (TEM sizes of Gd_2O_3 : 28 nm; SiO_2 : 128 nm; IONPs: 12 nm), and granulometric techniques. For IONPs, the grafting efficiency (30-100 %) do not impact on the colloidal stability and relaxivity properties of the so-functionalized NPs. **Conclusion:** Three dispersions of Amylovis-functionalized metal nanoparticles (Gd_2O_3 , metal-complexed SiO_2 , and IONPs) were successfully synthesized. Their surface functionalization and nanometric sizes (all under 200 nm) were confirmed. This work successfully lays the groundwork for developing targeted MRI contrast agents to improve the detection of senile plaques in Alzheimer's disease.



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sciforum-147604: Development of a method for obtaining and quality control of composites nanostructured with AgNPs particles for promising medical applications

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Introduction. This paper examines current aspects of the development and medical introduction of new disinfectants based on heterogeneous surface matrices exhibiting microbicidal activity, in the context of increasing resistance to existing drugs. A comprehensive approach is proposed for characterizing the properties of the synthesized matrix samples using both pharmacopoeial techniques and original methods. The purpose of this study was to develop, synthesize, and analyze materials with surface antimicrobial properties based on metallic silver nanoparticles (AgNPs). The study objects included: A nanodispersion containing metallic silver particles (AgNPs) synthesized by the citrate method using a 2 mM AgNO_3 solution (pH 5.4), 0.15 M sodium citrate, and 0.15 M glucose at 60°C; The formation of AgNPs was monitored by UV-Vis spectroscopy by sampling aliquots every 5 minutes during synthesis; A heterogeneous solid medical Paraffinum served as a model material with . It was prepared by adding an AgNPs suspension to molten paraffin (approximately 0.5 cm layer), continuously heated by a horizontal element, using spraying under mixing mimicking vortex water-oil emulsification. After synthesis, the nanostructured heterogeneous paraffin (NGP) sample was left to solidify completely. To assess the quality of both the nanodispersion and NGP, the following methods were applied: Dynamic Light Scattering (DLS, Zetasizer Nano ZS), UV-Vis spectroscopy (Agilent Cary 300), and surface diffuse reflection analysis. **Results.** The AgNPs in the nanodispersion exhibited an average particle size of approximately 150 nm (intensity distribution). The UV absorption peak at 440 nm corresponds to surface plasmon resonance and 4d–5sp interband electronic transitions. Chemometric analysis of speckle patterns formed by diffuse reflection from the heterogeneous surface provided a unique descriptor distribution enabling qualitative identification. **Conclusions.** The results may be valuable for the pharmaceutical industry in the synthesis, quality control, and application of new bactericidal systems. **Funding:** This research was supported by a grant from the RUDN University Strategic Academic Leadership Programme No. 033320–2-000.



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sciforum-152349: Fluorescent Carbon Dots: Emerging Multifunctional Platforms for Drug Delivery and Bioimaging

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Introduction: Carbon Dots (CDs) have emerged as promising nanomaterials for pharmaceutical and diagnostic applications due to their tunable fluorescence, biocompatibility, and potential for surface functionalization. Their dual applicability as drug delivery nanocarriers and fluorescent probes for bioimaging makes their physicochemical characterization crucial for advancing biomedical research. **Methods:** CDs were synthesized using citric acid as the carbon precursor through two distinct approaches: thermal pyrolysis in an oil bath at 200 °C for 30 min and a hydrothermal method at 200 °C for 4 h in the presence of urea as a nitrogen source. The nanostructures were characterized by transmission electron microscopy (TEM), UV-Vis absorption spectroscopy, photoluminescence spectroscopy, Fourier-transform infrared spectroscopy (FTIR), Raman spectroscopy, and zeta potential analysis. **Results:** TEM analysis revealed spherical and homogeneous particles with an average diameter of 3.0–3.5 nm, consistent with the size range of quantum dots. Optical characterization showed stable photoluminescence, with absorption maxima at 333–350 nm and excitation-independent emission attributed to ordered sp^2 domains. Nitrogen doping significantly enhanced fluorescence intensity, increasing quantum yield and improving stability within a physiological pH range (4.5–9.5). FTIR spectra confirmed the presence of surface functional groups such as C=O, C–N, and C–OH, while Raman analysis revealed the characteristic D and G bands of graphitic carbon. Zeta potential values of approximately –30 mV indicated high colloidal stability and abundant anionic groups favorable for further functionalization. **Conclusions:** The combination of small size (10 nm), high photostability, tunable fluorescence, and negative surface charge highlights the multifunctional potential of CDs. These features support their application both as drug delivery systems, responsive to physiological conditions, and as fluorescent probes for bioimaging, reinforcing their relevance as advanced platforms in therapeutic and diagnostic contexts.



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sciforum-151530: Formulation, Optimization and Evaluation of Mebendazole Nanosuspension: An Approach to Enhance Dissolution

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Objectives

The objective of this study is to develop a mebendazole (MBZ) nanosuspension designed as an immediate-release dosage form to improve solubility and bioavailability.

Material and Methods

MBZ, classified as a BCS Class II drug, demonstrates low bioavailability (10%) due to its limited solubility (0.035 mg/mL). The wet-media milling technique was utilised to reduce particle size, which subsequently increased surface area and dissolution rate. Polyvinyl alcohol (PVA) has been chosen as the stabiliser to improve formulation stability and inhibit particle aggregation. A comprehensive factorial design was employed to optimise critical process parameters, resulting in a nanosuspension characterised by an optimized mean particle size and a polydispersity index (PDI).

Results:

The optimised formulation exhibited an 8.72-fold enhancement in solubility and achieved over 98% drug release within 60 minutes *in vitro*, markedly surpassing both pure MBZ and existing marketed formulations. The formulation demonstrated a high entrapment efficiency of 96.21% and a drug content of 97.53%, thereby ensuring optimal drug loading. The successful conversion of MBZ into the amorphous form was confirmed through differential scanning calorimetry (DSC). The freeze-drying process enhanced dissolution properties while preserving formulation integrity, stability, and long-term viability. The solubility of the nanosuspension exhibited a significant increase in both aqueous and acidic media, effectively addressing the dissolution-limited absorption of MBZ.

Conclusions:

The findings indicate that nanosuspension technology represents a viable approach for enhancing the dissolution of poorly soluble drugs. The research highlights the potential use of nanosuspensions in drug delivery, especially for BCS Class II compounds, providing an effective formulation strategy to improve pharmacokinetic performance, stability, safety, and therapeutic results.



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sciforum-151948: Hybrid Lipid-Polymeric Nanoparticles for Enhanced Bioavailability of Vardenafil in Hepatic Encephalopathy Prevention: A Drug Repurposing Approach

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Hepatic encephalopathy (HE) is a severe neurological complication of liver failure with limited therapeutic options. Vardenafil dihydrochloride (VD), a PDE5 inhibitor, used for erectile dysfunction, shows potential for HE prophylaxis through cGMP elevation and neuroprotection, but it suffers poor oral bioavailability due to low solubility and first-pass metabolism. This study aimed to develop hybrid lipid-polymeric nanoparticles (HLPNPs) with piperine as a bioavailability enhancer for VD repurposing in HE prevention.

HLPNPs were prepared using homogenization/ultrasonication technique with glyceryl tripalmitate and Eudragit RS100. The helper polymer type (oleic acid, chitosan, sodium alginate) was evaluated using a one-factor experimental design on each of the particle size, polydispersity index, zeta potential, and entrapment efficiency. In vitro release studies, pharmacokinetics and therapeutic efficacy tests in a thioacetamide-induced HE mouse model were conducted.

Oleic acid emerged as the optimal helper polymer, yielding HLPNPs with 128 ± 2.8 nm particle size, 0.173 ± 0.07 PDI, -32 ± 1.67 mV zeta potential, and $93 \pm 1.8\%$ entrapment efficiency. In vitro release showed sustained VD release ($\sim 70\%$ over 72h) following Korsmeyer-Peppas kinetics. Pharmacokinetic studies revealed a remarkable 9-fold improvement for the optimized formulation compared to standard VD, with C_{max} increasing from 9 ng/mL to 22 ng/mL. In the HE mouse model, the optimized formulation significantly improved liver enzymes (ALT, AST), reduced ammonia levels, and enhanced hippocampal BDNF, cGMP, GluR1, and P-CREB levels compared to standard VD treatment.

The piperine-enhanced HLPNPs successfully overcame VD's bioavailability limitations and demonstrated superior therapeutic efficacy in HE prevention. This innovative drug repurposing approach combining nanotechnology with bioavailability enhancement offers a promising strategy for expanding VD's therapeutic applications beyond erectile dysfunction to neurological conditions.



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sciforum-150864: Innovative nanoplatforms with simultaneous triple drug co-delivery for improved synergistic therapeutic effects

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Nanotechnology has emerged as an innovative tool capable of overcoming the limitations of traditional drug delivery systems by enabling the manipulation of materials at the nanometric scale, giving them unique properties such as enhanced solubility, increased stability, and drug targeting to the therapeutic site of action. Among the most significant advantages that nanosystems have, is the fact that they allow the co-encapsulation of multiple drugs within a single nanosystem, harnessing their synergistic effects, contributing significantly to the reduction of potential side effects associated with conventional multiple therapy and with a potential impact on patient compliance. This literature review explores studies analyzing the potential of simultaneous delivery of three drugs within different types of nanosystems, for the treatment of chronic and infectious diseases, namely rheumatoid arthritis, psoriasis, human immunodeficiency virus infection, *Helicobacter pylori* infection, and anti-inflammatory therapies, as well as conditions such as secondary degeneration following neurotrauma, being the first of its kind, and filling an existing gap in the scientific literature. Parameters such as particle size, polydispersity index, zeta potential, encapsulation efficiency, and *in vitro* and *in vivo* efficacy and safety assays consistently demonstrated efficient co-encapsulation of multiple drugs with potential pharmacological synergy, controlled and prolonged drug release, and the capacity for therapeutic site-specific targeting, thereby increasing bioavailability and enabling the reduction of systemic adverse effects. While transition into clinical practice still faces regulatory hurdles, and in-depth long-term safety assessments are needed, overall nanosystems could play a leading role in the future of nanomedicine towards more effective and personalized therapies.



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sciforum-152170: Next-Generation Wound Dressings: Bioactive Nanocomposite Fiber Coatings Evaluated in an Albino Rat Model

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Wound healing is complex process and is subject of intense research. Use of plants against diseases is in practice from decades. In present study, green ZnO NPs dressings has been evaluated for antibacterial (*in vitro* analysis on *Bacillus subtilis*, *Lactobacillus acidophilus*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli* and *Klebsiella aerogenes*), hemolytic (*in vitro*), cytotoxic activity (MTT assay), water-solubility, biodegradability, capability to absorb large amounts of wound exudates and *in vivo* activity (on albino rats of both genders against incisionwounds). SEM confirmed successful incorporation of ZnO NPs into dressings. Broad peak at 3307 cm⁻¹ corresponded to O-H stretch in FTIR spectra, with new absorption peaks at 1600, 2000, and 2500 cm⁻¹ while intensity of C-O stretch was reduced which confirmed the degradation of dressings. ZnO NPs bandages contributed to high-water uptake, minimum hemolytic activity (19.8±0.88%) towards human RBCs at lowest dose (125µg/mL), decrease in HepG 2 cells viability with increased ZnO NP concentration, maximum inhibition of *L.acidophilus* (24±0.94 mm) and minimum activity against *K.aerogenes* (8±0.01 mm). On day 7, 60µg/mL of ZnO NPs embedded bandage showed highest healing activity in female rats (57.5%) as compared to male rats (45%), followed by bandage with 20µg/mL ZnO NPs (15% and 25 % healing in female and male rats). After 14 and 21 days, bandage with 10µg/mL nanoparticles showed 87.5% and 82.5% healing in male and female rats and 90% wound closure in both genders respectively. Bandage without nanoparticles, with PV and with 30µg/mL-50µg/mL nanoparticles showed lesser healing activity. Histological analysis of paw skin showed no inflammation but with reepithelization, collagen deposition, granulation tissue fibroblast maturation and neovascularization by bandage which was coated with least amount of green nanoparticles. Outcomes of current work indicate a clear improvement over conventional dressings and warrant further exploration of their unique properties for enhanced wound healing in clinical settings.



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sciforum-152341: Optimizing Graphene Oxide Dispersion in DMSO via Ultrasonic Processing: A UV-Vis-NIR Spectroscopic Study for Biomedical Applications

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This study investigates graphene oxide (GO) dispersions in dimethyl sulfoxide (DMSO) as an intermediate platform for developing nanocarriers for biomedical applications. DMSO's high polarity and hydrogen bonding ability make it an effective medium for optimizing GO's dispersion and optical properties before transferring to biocompatible systems.

GO was synthesized from glucose, and dispersions in DMSO (0.125–1.5 g/L) were prepared using mechanical stirring and ultrasonic homogenization. UV-Vis-NIR spectroscopy (200–3000 nm) was used to characterize the dispersions. Key parameters like transmittance, absorption coefficients, and bandgap width were calculated.

Controlled ultrasonic treatment produced stable dispersions with an increased molar extinction coefficient ($\epsilon_m \approx 14 \text{ l} \cdot \text{g}^{-1} \cdot \text{cm}^{-1}$), indicating effective exfoliation and a rise in sp^2 domains. The constant optical bandgap ($E_g \approx 3.95\text{--}4.0 \text{ eV}$) confirmed the process was non-destructive, preserving GO's functional integrity. Spectroscopic data revealed specific GO-DMSO interactions, such as hydrogen bonding, which ensure colloidal stability.

The established dispersion patterns and spectral behaviors in DMSO can be translated to biocompatible media like aqueous buffers or amphiphilic polymers (e.g., Pluronic F127), maintaining the material's stability and optical properties. This protocol provides a universal platform for preparing GO dispersions suitable for drug delivery systems, contrast agents, and optical biosensors. The original contribution demonstrates that DMSO as an intermediate enables controlled GO dispersion and the formation of optical parameters reproducible in pharmaceutical systems.



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sciforum-151302: Rebamipide Loaded Ethosomes as a Potential Trans-Eyelid Delivery

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Dry Eye Disease (DED) is a multifactorial condition characterized by tear film instability, leading to discomfort, visual disturbances, and potential ocular damage. Conventional treatments, such as topical eye drops, suffer from poor bioavailability due to rapid clearance, low drug penetration, and frequent dosing requirements, which negatively impact patient compliance. This study aimed to develop and evaluate a novel ethosome-based formulation for the trans-eyelid delivery of rebamipide, a mucoprotective and anti-inflammatory drug, to enhance its solubility, stability, therapeutic efficacy, and patient adherence.

The optimized ethosomal formulation (E6) exhibited a particle size of 242 ± 11.8 nm polydispersity index (PDI) of 0.221 ± 0.003 , and an entrapment efficiency (EE%) of $94.5 \pm 0.6\%$, confirming its suitability for drug delivery. Fourier Transform Infrared Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC) confirmed the stability of rebamipide within the ethosomal system, while X-ray Diffraction (XRD) revealed a transition to an amorphous state, enhancing drug solubility. Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) demonstrated a smooth, spherical morphology with uniform particle distribution. Stability studies showed that E6 maintained its physicochemical properties over 180 days at both 4°C and ambient temperature.

In vitro drug release studies indicated a sustained release profile over 12 hours, with a controlled release pattern fitting the zero-order kinetic model. Ex vivo permeation studies revealed that E6 significantly enhanced drug penetration through the eyelid skin, achieving a flux of $0.4285 \text{ mg} \cdot \text{cm}^{-1} \cdot \text{h}^{-1}$ and a permeability coefficient of $0.1071 \text{ cm} \cdot \text{h}^{-1}$, approximately three times higher than the control formulation. These findings highlight the potential of ethosome-based trans-eyelid delivery as an effective alternative to conventional ocular drug delivery, providing prolonged drug retention, reduced dosing frequency, and improved patient compliance.

Overall, this study supports the development of rebamipide-loaded ethosomes as a promising strategy for DED management. Further in vivo evaluations and clinical trials are recommended to establish their therapeutic efficacy, safety, and long-term adherence benefits.



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sciforum-148243: Synergistic triple drug co-loaded nanoplatforms for improved cancer treatment

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Cancer remains one of the leading causes of death worldwide. Current therapies often have relevant limitations, including low selectivity to tumor tissues, leading to systemic toxicity, and treatment resistance development. In recent years, however, nanotechnology has emerged as a promising approach to improving drug delivery, offering enhanced tumor targeting, better pharmacokinetics and fewer side effects. Additionally, making use of different pharmacological action mechanisms, delivering more than one drug molecule simultaneously can lead to synergistic or additive therapeutic effects. In this context, a scientific literature review was performed, exploring experimental studies that use nanocarriers for triple drug co-delivery in cancer treatment. The analyzed studies employed well-established chemotherapeutic agents and non-classical anticancer agents, such as 2'-deoxy-5-fluorouridine 5'-monophosphate, 5-fluorouracil, alpha-lipoic acid, camptothecin, chlorambucil, cisplatin, combretastatin A4, crizotinib, curcumin, doxorubicin, ellagic acid, erastin, fluvastatin, gemcitabine, honokiol, irinotecan, leucovorin, palbociclib, paclitaxel, pemetrexed, rosuvastatin, sildenafil, silybin, small interfering RNA against programmed death-ligand 1 platinum-based cross-linker, tariquidar, verteporfin, and zinc(II) phthalocyanine. These therapeutic agents were formulated within nanocarriers such as polymeric nanoparticles, polymeric micelles, dendrimers, PEGylated liposomes, lipid-polymer hybrids and inorganic nanoparticles. Each nanocarrier type offers specific advantages in terms of drug loading, drug release control and targeting ability. Overall, this review supports the idea that triple-drug nanocarrier-based strategies are powerful, evolving tools for developing more effective cancer therapies. These strategies offer enhanced synergistic effects, increased therapeutic precision and the potential to modulate the tumor microenvironment.



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sciforum-151489: Targeting P-glycoprotein with Functional Excipients: Development of Irinotecan Nanoparticles for Enhanced Chemotherapeutic Efficacy

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Introduction and Background: Multidrug resistance (MDR) is a major obstacle in cancer treatment, often caused by the action of permeability glycoprotein (P-gp) efflux pumps which reduce drug accumulation in cancer cells. To develop and optimize a nanoformulation of Irinotecan using excipients known for their P-gp inhibitory potential, aiming to overcome MDR in cancer therapy.

Methods: Nanoparticles were prepared and optimized employing a 3-factor, 2-level factorial design focusing on hydroxypropyl methylcellulose (HPMC) concentration and the number of preparation cycles. Particle size, polydispersity index (PDI), and entrapment efficiency were evaluated. Characterization was performed using Differential Scanning Calorimetry (DSC) and X-Ray Diffraction (XRD) to confirm molecular dispersion. In vitro P-gp inhibition was assessed in Caco-2 cells with ELISA analysis, and in vivo efficacy was evaluated through pharmacokinetic studies in rats.

Results: The optimized Irinotecan nanoparticles exhibited a particle size of 201 nm, PDI of 0.100, and entrapment efficiency of 91%. DSC and XRD confirmed the molecular dispersion of the drug within the freeze-dried nanoparticles. In vitro studies demonstrated significant P-gp inhibition, with the nanoformulation requiring nearly half the concentration to achieve similar effects compared to the free drug. In vivo studies showed enhanced P-gp inhibition, indicated by improved maximum plasma concentration (C_{max}) values.

Conclusion: Excipients-based Irinotecan nanoparticles effectively inhibit P-gp activity, providing a promising nanoformulation strategy to overcome multidrug resistance in cancer treatment.



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Session 11. Formulation, Drug Delivery and Controlled Release

sciforum-152192: Efficient Delivery of Genetic Constructs to Uterine Fibroid Cells Using Peptide Nanocomplexes

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Uterine fibroids are a prevalent clinical concern in gynecology, and current surgical interventions, myomectomy and hysterectomy, pose risks of complications and potentially compromise reproductive function. Given the limitations of conventional treatments, there is a significant need for organ-sparing alternatives, such as gene therapy.

This study addresses the development of non-viral gene delivery strategies for uterine fibroids. Traditional viral vectors present substantial risks, including immunogenicity, insertional mutagenesis, and limitations in repeated administration. Non-viral systems for uterine fibroid therapy remain relatively unexplored despite their potential for localized treatment and reduced systemic effects.

We developed a novel ternary peptide-based system incorporating both cationic and anionic peptide components to address limitations of conventional binary complexes. The inclusion of anionic peptides enhances complex stability via improved charge distribution, promotes efficient cellular internalization, and reduces nonspecific interactions with biological constituents. Our optimization strategy focused on two key parameters: minimizing complex formation volume while maintaining therapeutic DNA payload, and determining optimal charge ratios between DNA, cationic and anionic peptides.

Comprehensive physicochemical characterization included analysis of hydrodynamic properties via dynamic light scattering (DLS), surface charge assessment via zeta potential measurements, DNA binding capacity evaluation, and investigation of release kinetics. Biological evaluation demonstrated preserved cellular viability and significantly enhanced transfection efficiency in both cell culture models and ex vivo fibroid tissue. The system achieved consistent particle sizes below 200 nm with favorable surface charge characteristics for cellular uptake.

These findings suggest that this optimized ternary peptide system represents a robust and efficient platform for gene delivery to uterine fibroid cells, offering a promising organ-preserving approach for translational gene therapy applications.



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sciforum-140536: Formulation and Evaluation of Nitazoxanide Floating Microsphere

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Nitazoxanide is a broad-spectrum antiparasitic and antiviral agent widely used in the treatment of diarrhoea caused by protozoa such as *Giardia lamblia* and *Cryptosporidium parvum*. Despite its clinical effectiveness, Nitazoxanide suffers from certain pharmacokinetic limitations, including poor aqueous solubility, low oral bioavailability, and a short plasma half-life. To address these challenges, a gastro retentive drug delivery system in the form of floating microspheres was developed to enhance the drug's bioavailability and prolong its residence time in the stomach. The floating microspheres were prepared using the solvent evaporation method, in which HPMC and Ethyl cellulose were used as a polymer, DCM and ethanol used as a solvent, Tween 80 is used as a surfactant. Six formulation batches were fabricated and evaluated for parameters such as micromeritic properties, particle size, Percentage entrapment efficiency, percentage yield, Percentage *in-vitro* buoyancy behavior, surface morphology, zeta potential and *in vitro* drug release profile. The physicochemical properties of microsphere strongly affected by the presence of drug/polymer ratios. Among all formulations, batch F5 shows highest % entrapment efficiency (78.1%), % yield (84.1%), *In-vitro* buoyancy (87.9%), Zeta potential of -20.3mV and moderate particle size. The drug is released upto 12 hrs. and 76.02% of drug has been released from the formulation representing the controlled release nature.



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sciforum-150690: Nanocarriers based on methyluracil derivatives for the redox-mediated delivery of photosensitizers to cancer cell

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In recent decades, new methods of cancer treatment have been developed. One of these methods is photodynamic therapy (PDT), which is non-invasive and based on the generation of reactive oxygen species (ROS) when light interacts with photosensitizers (PS). However, photosensitizers often have low solubility and reduced bioavailability under physiological conditions. To address this issue, nanocarriers have been created to deliver photosensitizers more effectively, increasing the depth of penetration into cellular structures and enhancing the therapeutic effect of PDT.

The paper presents nanocarriers obtained through the nanoemulsion polymerization reaction between homologous methyluracil derivatives (4-(3,6-dimethyluracil)-butyl acrylate or 3-(3,6-dimethyluracil)-propyl acrylate) and N,N'-bis(acryloyl)cystamine. These methyluracil derivatives form the shells of the nanocarriers, while N,N'-bis(acryloyl)cystamine, dissolved in DMSO, acts as the dispersed phase to form a hydrophobic core. Porphyrin derivatives with various substituents at the meso-position are encapsulated within the core of these nanocarriers. According to transmission electron microscopy data, carrier sizes ranged from 50 to 200 nanometers (nm), and nanocarriers containing a glycoporphyrin derivative had the smallest hydrodynamic diameters.

The cores, formed by N,N'-bis(acryloyl)cystamine, contain disulfide bonds that can be reduced by intracellular antioxidants such as glutathione. These antioxidants are often found in tumor environments. The reaction of reducing the disulfide bond leads to the disintegration of the particles and the release of PS. This process has been confirmed by the fluorescence method, which shows an increase in emission intensity over time when glutathione is added to the carrier solution.

The formation of singlet oxygen upon irradiation of nanocarriers with PS was confirmed using 1,3-diphenylisobenzofuran (DPBF) and UV spectroscopy. PS in nanocarriers based on 4-(3,6-dimethyluracil)-butyl acrylate generated singlet oxygen at almost twice the rate of individual PS.



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sciforum-151871: Pectin Films Containing Propranolol-Loaded Nanocapsules for Infantile Hemangioma Treatment

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Hemangioma is an abnormal growth of blood vessels in the skin, forming a benign tumor, mostly common in infants and children. Propranolol (PRO) is a non-selective beta-blocker used as an antihypertensive that has shown regression in infantile hemangiomas. Its oral administration comes with adverse effects, including a high risk for asthmatic patients, and only 25% of the administered dose is bioavailable. With that in mind, the incorporation of PRO into nanocapsules (NCs)-based polymeric films provides protection against degradation, prolongs its half-life, allows controlled release, and modulates its skin permeation/penetration. Given the above, this study incorporates propranolol Eudragit RL®100 nanocapsules in pectin films, obtained by the solvent casting method, and characterizes them for porosity and intumescence. Nanocapsules presented 151 ± 7.86 nm, 0.134 ± 0.01 PDI, and 25.64 ± 4.9 zeta potential. The pectin films (1%) were homogeneous and transparent. The porosity ratio was determined by the amount of absorbed solvent by the film sample after immersion in ethanol. Samples were obtained from vehicle formulation, free drug, NC-PROP, and blank NC films. The results obtained after 24h were $55.93 \pm 3.13\%$, $49.91 \pm 0.56\%$, $42.49 \pm 2.05\%$, $41.74 \pm 2.5\%$, respectively. This indicates that the NCs interact in a way that modifies the pores and creates a more effective barrier than the vehicle or free drug form. For intumescence, the same method was applied, apart from the solvent being a pH 7.4 buffer, but all the film samples disintegrated and dissolved in the buffer, indicating a biodegradable matrix. The incorporation of PRO-loaded nanocapsules into pectin films resulted in homogeneous and biodegradable matrices with reduced porosity and promising barrier properties. These characteristics suggest that NC-PROP films can provide a controlled and localized drug release, potentially reducing systemic adverse effects associated with oral administration. Overall, this approach represents a promising strategy for the topical treatment of infantile hemangiomas.



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sciforum-146387: Aloe-emodin-Loaded Microemulsion Based Herbal Gel: Design, Optimization, and Therapeutic Evaluation for Diabetic Wound Healing

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Phytomedicine has moved beyond being seen only as a folklore remedy and has become an important part of modern therapeutics. Aloe-emodin (AE), a phytoconstituents present in Aloe, is a naturally occurring anthraquinone, exhibits notable anti-inflammatory, antimicrobial, and wound-healing properties. However, its clinical potential is limited by poor aqueous solubility and inadequate skin permeability. To overcome these challenges, an AE-loaded gel (AMEG) was developed to enhance topical delivery and therapeutic efficacy in diabetic wound management. The formulation was optimized using a D-optimal mixture design, selecting Capryol 90 as the oil phase, Labrasol and Tween 80 as surfactants, and Transcutol P as the co-surfactant. A stable gel matrix was formed by incorporating konjac glucomannan (KGM) and carbopol 940, improving skin adherence and drug retention. The optimized AMEG demonstrated nanoscale droplet size, high zeta potential, and excellent clarity. *In vitro* and *ex vivo* studies confirmed sustained drug release and enhanced transdermal penetration. *In vivo* application in diabetic rats significantly accelerated wound healing, accompanied by modulation of key inflammatory and oxidative markers, including IL-1, IL-6, NF- κ B, TNF- α , MDA, and AGEs. Histopathological assessments revealed full re-epithelialization and organized collagen deposition. The combined effect of AE and KGM underscores the potential of AMEG as a promising, non-invasive therapeutic approach for diabetic wound care, leveraging the advantages of herbal compounds in enhancing healing and reducing inflammation.



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sciforum-152001: Antioxidant and toxicological effects of verbenone enhanced with cyclodextrin and lysine in diclofenac induced oxidative stress mice

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Oxidative stress is a pathological condition that plays crucial roles in the pathogenesis of various diseases. This study evaluated the antioxidant and toxicological effects of verbenone enhanced with cyclodextrin and lysine in diclofenac induced oxidative stress mice. Adult Swiss mice (35) were randomly distributed into seven (7) groups, induced with oxidative stress and orally administered verbenone, lysine, cyclodextrin, verbenone-lysine, and verbenone-cyclodextrin at 200 mg/kg body weight for seven (7) days. Cyclodextrin treatment significantly increased (p0.05) total cholesterol, low density lipoprotein cholesterol (LDL), high density lipoprotein cholesterol (HDL), and triglycerides compared with diclofenac control. No significant alterations (p0.05) were observed in very low density lipoprotein cholesterol (VLDL), while a significant increase (p0.05) was observed with diclofenac treatment in liver triglycerides. No significant alterations (p0.05) were observed with atherogenic index while cyclodextrin significantly increased cardiac index and coronary artery index. Plasma protein and catalase activities decreased significantly (p0.05) in all treatment groups. No significant alterations (p0.05) were observed in malondialdehyde and liver superoxide dismutase. Glutathione peroxidase activity decreased in plasma for verbenone, cyclodextrin, and verb-cyclodextrin, but increased in the liver with lysine and cyclodextrin treatments. Liver albumin and total bilirubin were elevated in treatments, while gamma-glutamyl transferase activity significantly increased (p0.05) across all groups except with verbenone treatment. Histopathology revealed periportal inflammation in verb-lysine, and while liver and kidney architecture in verb-cyclodextrin and verbenone groups was preserved. The study reveals complex interactions between diclofenac-induced oxidative stress and the modulatory effects of verbenone, lysine, and cyclodextrin. Verbenone and the various mitigated oxidative damage, with cyclodextrin conjugation presented more safety profile compared to lysine conjugation. The combination of verbenone and lysine or cyclodextrin may provide valuable insights into the modulation of renal and hepatic functions under oxidative stress conditions.



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sciforum-146590: Citrus flavanone (naringenin)-infused transferosome based gel: Development, optimization, characterization with an exploration of diabetic wound healing potential through an integration of network pharmacology, *in vitro* and *in vivo* studies

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Flavonoids are widely used natural phenolic compounds, which have shown potential role in wound healing. Many pre-clinical studies have indicated that flavonoids are one of the most promising and important group of natural compounds which can be used to treat acute as well as chronic wounds. Flavonoids can be classified as flavones, isoflavones, flavonols, flavanols, flavanones and anthocyanins respectively. Naringin, the glycone part and naringenin the aglycone part falls under the broad umbrella of flavonoid class (flavanones) which are majorly obtained from various citrus fruits like lemon, orange, grapefruit. Several therapeutic roles have been documented for naringenin, such as anti-inflammatory, antioxidant, antiulcer, anticancer, wound healing activities. Due to challenges in solubility, it is crucial to encapsulate these compounds using nanotechnological platform to deliver and make them bioavailable for the treatment of several diseases. Nanocarriers like transferosomes act as self-adaptable ultra-deformable flexible bilayer vesicles composed of phospholipid and edge activators along with hydration media. The present study has focused on the beneficial role of the flavonoid naringenin with a special emphasis on naringenin encapsulated transferosomal gel towards healing of different diabetic wound conditions and exploring their underlying mechanisms. Quality by design (QbD) employing design expert software to optimize transferosomes and further Dynamic light scattering (DLS) studies, Field emission scanning electron microscopy (FESEM), Fourier-transformed infrared spectroscopy (FT-IR) analysis, X-ray diffraction (XRD) studies, Rheology studies, Percentage entrapment efficiency followed by *In vitro* drug release studies for naringenin encapsulated transferosomal gel has been evaluated. Development of naringenin embedded transferosomal gel has been carried out along with its *in vitro* antioxidant, antimicrobial activity evaluation followed by *in vivo* wound healing studies.



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sciforum-147938: Conventional and Galactosylated Liposomal Formulations of Ellagic Acid for the Modulation of Cellular Senescence

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Ellagic acid (EA) is a natural polyphenolic compound mainly present in *Punica granatum L.* It has gained increasing interest for its antioxidant and anti-senescence properties, with documented benefits in models of cardiovascular, renal, and neurodegenerative aging. However, its clinical application is hindered by very low aqueous solubility (9.7 µg/mL), poor bioavailability, and limited stability.

This study aimed to overcome these limitations by developing a liposomal formulation (LP-EA), further functionalized with a galactose derivative (Gal-LP-EA) for selective delivery to senescent cells. This targeting strategy exploits the overexpression of β -galactosidase, which cleaves the galactose-liposome bond, enabling the intracellular release of EA specifically in pathological cells.

LP-EA and Gal-LP-EA were prepared by thin-film hydration method and physicochemically characterized for particle size, polydispersity index (Pdl), zeta potential, morphology, and encapsulation efficiency (EE%). Stability was assessed over 30 days at controlled temperatures, and *in vitro* release profile was investigated using the dialysis bag method. Passive permeability across the blood-brain barrier (BBB) was evaluated by PAMPA test.

Encapsulation of EA into LP increased its solubility by approximately 56-fold. LP-EA and GAL-LP-EA showed size, Pdl and Zeta potential of 113.2 ± 0.91 nm, 0.21 ± 0.00 and -24.57 ± 0.43 mV and 110.8 ± 0.17 nm, 0.21 ± 0.02 and -24.04 ± 0.04 mV, respectively. EE% was around 80% for both formulations. The physicochemical properties were stable through the study period. Moreover, LP provided a sustained and gradual release over 24 h (~30%), avoiding the burst effect observed for EA solution (52% at 2h), following the Fickian diffusion mechanism. Liposomal formulations significantly enhanced EA BBB permeation, as evidenced by an approximately one order of magnitude increase in the permeability coefficient.

These results indicate that LP improved EA solubility, stability and controlled release, facilitating its transport across the BBB. Thus, GAL-LP-EA could represent a promising nanomedicine-based strategy for age-related diseases.



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sciforum-152325: Design and Characterization of Novel Nanoemulsion Formulation of Cannabinoid using Nanotechnology Platform for Targeted Ophthalmic Drug Delivery

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Purpose

This research aims to develop a stable Nanoemulsion formulation for a challenging, water-insoluble, and thermally, oxidatively, and photolytically unstable active pharmaceutical ingredient (API) for ophthalmic use, specifically to help reduce intraocular pressure (IOP) and provide neuroprotection. The cannabinoid API has shown great potential in treating glaucoma by targeting the endocannabinoid system (ECS) to lower IOP and provide valuable neuroprotection.

Method

The solubility of the cannabinoid in various oils was systematically assessed. Placebo trials were conducted to identify the appropriate stabilizer and its concentration. To mitigate oxidation, low peroxide-grade sesame oil, and nitrogen/argon-purged water were used throughout the process. Nanoemulsion was prepared under a nitrogen atmosphere. Reduction of particle size was accomplished utilizing a Microfluidics M110-P under optimized pressure and number of passes. Antioxidants were evaluated to inhibit the oxidation of the API. Various packaging materials were evaluated for stability.

Results

Sesame oil exhibited the most pronounced solubilizing capability for the API. Tween 80 effectively stabilized the Nanoemulsion, resulting in a particle size of approximately 150 nanometers. Treatment via a microfluidizer at a pressure of 25,000 PSI over five passes yielded the targeted particle size alongside a low polydispersity index and a narrow size distribution. The Nanoemulsion retained its particle size even after filtration through a 0.22 μm filter, experiencing minimal resistance. A synergistic combination of butylated hydroxyanisole /butylated hydroxytoluene and Vitamin A effectively mitigated the oxidation of the cannabinoid API. Containers composed of low-density polyethylene and high-density polyethylene demonstrated enhanced stability in comparison to polypropylene and amber glass containers.

Conclusion

This research proficiently formulated a stable Nanoemulsion for the ophthalmic delivery of the cannabinoid API, effectively mitigating issues related to its inadequate aqueous solubility and inherent instability. The findings provide valuable insights into the potential treatment of glaucoma using this novel Nanoemulsion formulation.



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sciforum-152260: Design of Aquasome-Based Systems for Brain-Targeted Delivery of DDL-920

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Alzheimer's disease (AD) remains one of the most difficult neurological disorders to manage, largely because existing treatments provide only modest benefit and most drug candidates fail to cross the blood–brain barrier (BBB) in effective amounts. DDL-920, a small molecule with neuroprotective activity, has shown encouraging preclinical effects, including a 45% improvement in spatial memory and a 38% reduction in amyloid plaque burden in transgenic mouse models. However, its clinical application has been limited by very low aqueous solubility (0.5 µg/mL), poor oral bioavailability (~12%), and minimal brain penetration (brain/plasma ratio 0.08). To overcome these challenges, aquasome-based nanocarriers were developed as delivery systems for DDL-920. The optimized formulation demonstrated favorable physicochemical characteristics, with a particle size of 152.3 ± 6.4 nm, zeta potential of -21.6 ± 2.3 mV, and an encapsulation efficiency of $82.4 \pm 3.5\%$. In vitro release experiments confirmed a sustained drug profile, with 74% release at 48 h, along with a 12-fold improvement in solubility compared to the free drug. BBB transport studies in hCMEC/D3 cells indicated a 4.3-fold higher permeability for the aquasomes, and in vivo testing revealed greater brain accumulation (2.6 ± 0.4 µg/g vs. 0.5 ± 0.1 µg/g). Behavioral evaluations in AD mice further showed superior memory recovery, with 65% improvement versus 28% for the free drug. Overall, these findings support aquasome technology as a promising platform for enhancing the therapeutic potential of DDL-920 in Alzheimer's disease.



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sciforum-150913: Design of Soy Lecithin Vesicle Nanocarriers: Impact of DPPC, DOPC, and Cholesterol on Bilayer Dynamics and Release Properties

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This study explores the preparation and characterization of soy lecithin vesicles modified with dipalmitoylphosphatidylcholine (DPPC), dioleoylphosphatidylcholine (DOPC), and cholesterol (CHO), focusing on how these compositional changes modulate bilayer fluidity and permeability. Large unilamellar vesicles (LUVs) with narrow size distribution were successfully obtained by the extrusion method, and unencapsulated ferricyanide was efficiently removed by gel chromatography on Sephadex. Remarkably, the incorporation of saturated DPPC enabled the formation of stable LUVs at room temperature, well below its gel-to-liquid crystalline phase transition temperature (~41 °C), a challenging task when using DPPC alone.

Bilayer fluidity was assessed using the fluorescent probe 6-propionyl-2-(N',N'-dimethyl)aminonaphthalene (PRODAN), while permeability was evaluated through the encapsulation and release of $K_4[Fe(CN)_6]$, a hydrophilic and electroactive molecule. Incorporation of the analyte did not affect vesicle assembly.

The highest bilayer fluidity was observed in Lec:Cho (1:1.6) and Lec:DPPC (1:2) systems, whereas Lec:DOPC mixtures were dominated by the ordering effect of DOPC.

Release studies revealed striking formulation-dependent differences. Complete release of $K_4[Fe(CN)_6]$ occurred in Lec:Cho (1:1.6), Lec:DPPC (1:2), and Lec:DOPC (1:1), while lecithin, Lec:DOPC (1:2), and pure DOPC vesicles showed partial release of 63%, 59%, and 22%, respectively. Notably, release rates were not directly correlated with release percentages: lecithin vesicles exhibited the fastest release (0.79%/min), whereas Lec:DOPC (1:1) vesicles were the slowest (0.19%/min). Overall, these results establish a clear correlation between bilayer fluidity and the release rate of ionic hydrophilic molecules, while also demonstrating that compositional tuning, particularly with DPPC, allows the design of lecithin-based nanocarriers with tailored permeability. This approach opens new opportunities for the development of vesicle-based delivery systems in nanomedicine using ionic analytes.



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sciforum-152400: Development and Characterization of a Stable Capsule Formulation containing Lyophilized (Freeze Drying) Monoclonal Antibody (mAb) for Oral Administration

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Purpose:

Monoclonal antibodies (mAbs) are significant biotherapeutic agents for various diseases. Their oral administration is hindered by instability in the gastrointestinal tract (GIT). Lyophilization offers a viable method for stable mAb formulation for oral use. This research discusses the development of a stable oral formulation of mAbs through optimized freeze-drying process.

Method:

mAb formulations were created in buffers of pH 5 (mAb1) and pH 7.4 (mAb2). Bulking agents, stabilizers, and their concentrations were identified for lyophilization. EDTA served as a protease inhibitor to reduce mAb degradation. The lead formulation was established using optimized freezing and drying parameters. Modulated differential scanning calorimetry (MDSC) assessed the glass transition temperature (T_g) and eutectic temperature (T_{eu}). Short-term stability up to 30 days was evaluated through assessments of cake appearance, reconstitution time, moisture content, purity, and related substances.

Results:

Trehalose showed superior cryoprotection as a bulking agent. Increasing trehalose concentration from 10% to 20% lowered the T_g of the lead formulation from -36°C to -34°C. The lyophilization cycle was optimized to 72 hours at freezing (-50°C), primary drying (-34°C), and secondary drying (20°C) with a pressure of 72mTorr. Methionine effectively stabilized the lyophilized mAbs, yielding minimal %Impurity. The addition of EDTA to the lead formulation with 20% trehalose did not influence T_g. MDSC findings indicated T_g's significance in maintaining low primary drying temperatures. Moisture content was below 3%. No significant differences in mAb concentrations were noted across various temperatures. However, Lyo-mAb1 exhibited greater stability compared to Lyo-mAb2, as indicated by %Purity data. Both formulations demonstrated %Impurity below 1%, indicating no process-related mAb degradation.

Conclusion:

This study provides critical insights for developing stable lyophilized mAb formulations, addressing stability issues related to enzymatic degradation and acidic pH in the GIT. Furthermore, the lyophilized formulation in enteric-coated capsules presents a promising method for oral mAb delivery.



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sciforum-146722: Development of Folate Receptor (FR- α) Mediated Nano Carrier Sustained Release Formulation for Ameliorating Colorectal Cancer

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Background: Colorectal cancer (CRC) remains a significant global health concern, ranking as the third most common cancer worldwide and the second leading cause of cancer-related mortality. The folate receptor- α (FR- α), a glycosylphosphatidylinositol (GPI)-anchored membrane protein, this overexpression presents a compelling opportunity for targeted drug delivery. **Aim:** This research aimed to develop an FR- α targeted nanocarrier system for the precise delivery of an anticancer agent, thereby minimizing off-target effects and systemic cytotoxicity to normal cells. **Methodology:** The targeted nanocarrier formulations were prepared by conjugating folic acid (FA)/Premetrexed and anticancer agents. Polymeric micelles were developed using an ethanol injection method to achieve a sustained-release formulation. Various excipients and block polymeric materials, including Pluronic P123, D1 lipids, and Transcutol HP, were utilized. The final formulations were rigorously characterized for particle size, surface charge (zeta potential), morphology, drug loading efficiency, and in vitro drug release kinetics. Furthermore, the cellular inhibitory effects and cytotoxicity were evaluated in vitro against colon cancer cell lines (CT-26 and HT29) and a normal human embryonic kidney cell line (HEK 293). **Results:** The formulations demonstrated nano size particle range (500 ± 25 nm) and a sustained drug release, with $\sim 67 \pm 5\%$ of the drug released over 72 hours in PBS (pH 7.4). High drug loading efficiency of $73 \pm 2\%$ was achieved, indicating a significant payload capacity. In cellular studies, the targeted formulations achieved 50% cell inhibition (IC₅₀) at a concentration of 0.250 μ M, significantly lower than the 0.585 μ M observed for non-targeted formulations. Critically, the targeted formulations exhibited markedly reduced cytotoxicity in the normal HEK 293 cell line. **Conclusion:** Our findings reveal that the FR- α targeted drug delivery system effectively ameliorates colon cancer, even at advanced stages. We also find the challenges in conjugation reaction, however more hypothetical experiments would be required to establish the chemical conjugation. Upon this issue we had used pemetrexed as potent antifolate ligand instead of folic acid.



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sciforum-150725: DNA/BSA binding study of *N*-benzylthiabendazole and its mononuclear silver(I) complex

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The antimicrobial properties of silver(I) ions have been recognized since ancient times. In recent decades, silver(I) complexes have been extensively studied for their antimicrobial activity. The ligand plays a crucial role not only in stabilizing the complex but also in modulating its physicochemical properties, such as solubility, lipophilicity, and the ability to release silver(I) ions under biological conditions. In addition to their broad spectrum of applications, silver(I) complexes are noted for their low toxicity to human cells and the remarkably low tendency of microorganisms to develop resistance. These characteristics make silver(I) complexes promising candidates for the development of novel antimicrobial agents, particularly in the fight against bacterial resistance to clinically used antibiotics. The possible mechanism of the antimicrobial activity of silver(I) complexes can be attributed to their interactions with biological molecules, including DNA and proteins. Thiabendazole is a benzimidazole derivative widely used as a pesticide, known for its potent antifungal and anthelmintic activities. Due to its favorable pharmacological profile, thiabendazole has attracted attention as a structural scaffold for the development of metal complexes with potential biological activity. In this study, we employed a benzyl-substituted derivative of thiabendazole, *N*-benzylthiabendazole (*N*-BzTBZ), as a ligand to synthesize a novel mononuclear silver(I) complex, $[Ag(N-BzTBZ)_2]CF_3SO_3$, exhibiting a distorted trigonal planar geometry. The binding affinity of both the free ligand and the synthesized complex with biologically relevant targets, bovine serum albumin (BSA) and calf thymus DNA (ct-DNA), were investigated using fluorescence emission spectroscopy.



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sciforum-150754: DNA/BSA binding study of iminodiacetate-based gallium(III) complexes

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Gallium(III) complexes have emerged as promising candidates in bioinorganic chemistry due to their structural versatility, stability, and ability to mimic iron in biological systems, which allows them to interact selectively with key biomolecules. Motivated by these properties, we synthesized two novel gallium(III) complexes, Na[Ga(ida)₂] $\cdot$ 2H₂O (1) and K[Ga(ida)₂] $\cdot$ 3H₂O (2), employing iminodiacetate (ida²⁻) as the ligand. The synthesis of these complexes was carried out in aqueous solution by reacting GaCl₃ with iminodiacetic acid (H₂ida) at 80 °C for 4 h in the presence of NaOH or KOH, respectively. Their structures were determined using IR and NMR (¹H and ¹³C) spectroscopy and further confirmed through single-crystal X-ray diffraction analysis. Building on this structural work, we investigated their interactions with bovine serum albumin (BSA) and calf thymus DNA (ct-DNA) using fluorescence emission spectroscopy to assess their binding affinity towards these biologically important molecules. Since serum albumin consists of three main domains (I–III), each subdivided into two subdomains (A and B), fluorescence competition experiments with site-specific markers were also performed to identify the preferred binding sites of the complexes. Eosin Y served as a marker for site I (subdomain IIA), ibuprofen for site II (subdomain IIIA), and digitoxin for site III (subdomain IB).



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sciforum-150730: DNA/BSA binding study of mononuclear gold(III) complex with azaconazole

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Nitrogen-containing aromatic heterocycles have garnered significant interest as essential scaffolds in the synthesis of bioactive compounds, owing to their broad applications in various pharmacological fields, including vitamins, herbicides, antifungal, antibacterial, and anticancer agents. Their unique structural and electronic properties allow them to interact effectively with biological targets, making them attractive ligands in the design of metal-based therapeutic agents. In the present study, azaconazole (acz) was employed for the synthesis of a mononuclear gold(III) complex, $[\text{AuCl}_3(\text{acz})]$. The complex was obtained by reacting equimolar amounts of potassium tetrachloridoaurate(III) and the acz ligand under reflux conditions for 3 h. In this complex, azaconazole coordinates monodentately to the Au(III) ion, while the remaining coordination sites in the square-planar geometry are occupied by chloride ions. The interaction between the synthesized gold(III) complex and calf thymus DNA (ct-DNA) was investigated using fluorescence emission spectroscopy in the presence of the intercalative agent ethidium bromide (EthBr) and the minor groove binder Hoechst 33258 (Hoe). Additionally, fluorescence competition experiments were performed using specific site markers, including eosin Y, ibuprofen, and digitoxin, to gain deeper insight into the binding sites on BSA. Eosin Y is known as a marker for site I (subdomain IIA), ibuprofen for site II (subdomain IIIA), and digitoxin for site III (subdomain IB).



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sciforum-124952: Evaluation of Alginate-Based Gels as Drug Carrier for Controlled Release of Spiramycin.

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Abstract

Introduction: Controlled drug delivery systems (DDS) are vital for enhancing therapeutic efficacy while minimizing side effects. Alginate (Al)-based materials have emerged as promising candidates due to their biocompatibility, gel-forming capacity, and ease of modification. This study aims to evaluate the performance of five novel Al-based formulations for the controlled rate of spiramycin release.

Methods: Five DDS were developed: spiramycin-Al hydrogel (SAH), spiramycin-acid activated montmorillonite-Al hydrogel (SMAH), spiramycin-poly lactide-acid activated MMT-Al hydrogel (SPMAH), and spiramycin-Al aerogel beads and films (SAAB and SAAF). Preparation involved drug encapsulation, incorporation of MMT as a sorbent, calcium chloride-induced crosslinking, coating with poly lactide, solvent exchange, supercritical drying, and drug impregnation. In vitro drug release was assessed via dissolution tests, and antimicrobial efficacy was evaluated against *E. coli*, *S. aureus*, and *E. faecalis*.

Results: Among the hydrogel formulations, SPMAH demonstrated the slowest release profile (20%), indicating effective sustained release, while SMAH and SAH showed higher release rates (>21% and >42%, respectively). SAAB and SAAF exhibited faster release in water compared to 50% Glycerol Ringer's solution. In antimicrobial assays, SAAB showed the most potent inhibition against all tested bacteria, highlighting its potential for effective antimicrobial action.

Conclusion: The results demonstrate that Al-based DDS, particularly SPMAH and SAAF, offer promising platforms for controlled spiramycin delivery. These systems may contribute to combating antimicrobial resistance by enabling sustained and targeted drug release. This study provides new insights into the development of advanced biomaterial-based DDS for antibiotics.



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sciforum-152350: Evaluation of the impact of IL on SLNs with Gelucire® or Precirol ATO®

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Nanosystems are gradually being more commonly used in a variety of applications, providing a new approach to therapeutics by improving the pharmacokinetic profile of several compounds. This has led to an increase in the search for bioinspired and sustainable materials for novel nanotechnology-based formulations with pharmaceutical and cosmetic purposes. For the delivery of bioactives to the skin, lipid nanoparticles, such as solid lipid nanoparticles (SLNs), have been thoroughly investigated. Their use is still being hampered, nevertheless, by issues with stability and drug loading during storage. Several methodologies, including the applicability of ionic liquids (ILs), may be used to improve this. These have proven to be a potential strategy due to the beneficial qualities that our group identified in earlier work, namely their capacity to enhance the colloidal stability of formulations. Using two different commercial lipids (Gelucire[®] 43/01 vs. Precirol ATO[®] 5) and an amino acid-based IL (2-hydroxyethyl)-trimethylammonium-L-phenylalaninate [Cho][Phe], this study aimed to assess the impact of the incorporation of the IL into the SLN, comparing both commercial lipids. After conducting stability tests and characterising these nanosystems in terms of size, zeta potential, and polydispersity index, SLNs with favourable properties were produced. The findings demonstrated that ILs helped to stabilise the nanoparticles and enhance their physicochemical characteristics for topical use. All things considered, choline-based ILs in combination with the creation of novel lipid nanocarriers from sustainable and bioinspired materials appear to create a new paradigm for skin delivery. These findings demonstrate that ILs can alter SLN size, which might enhance their physicochemical characteristics for topical use.



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sciforum-145257: Formulation of bioinspired functional hydrogel for the controlled drug release application

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Hydrogel is the first biomaterial designed for biomedical use. Polysaccharide based hydrogels are receiving much attention in the past few years, as intelligent materials due to their properties for biomaterials. One of the extensively studied approaches for controlling drug delivery is the encapsulation of drug within polymer chains which sluggish the release on the basis of its crosslinked network. Discontinuous volume variations in hydrogels upon changes of environmental parameters, like polymer composition, temperature, pH, etc., are named multi-responsive hydrogels.

Bioinspired functional hydrogels are prepared using chitosan and polyvinyl pyrrolidone with varying quantities of aminopropyl diethoxy methylsilane via solution casting protocol. Prepared hydrogels were evaluated by different physical and analytical characterization techniques. Swelling indices were examined in distilled water (247.52 g/g), different buffer and electrolyte solutions. Fourier transform infrared spectroscopy was conducted to confirm functional groups and to prove the proposed physical and chemical interactions between polymers and crosslinker. Thermogravimetric analysis was used to assess the response of prepared hydrogels against temperature and found maximum thermal stability up to 23.94% in terms of residue. Contact angle and X-ray diffraction analysis were conducted to investigate the hydrophilicity which was (71°) and crystalline properties, respectively. Extensively, in vitro studies including biodegradation, antimicrobial and cytotoxic properties were examined. Maximum biodegradation was achieved up to 6.4% in seven days and cytotoxicity was 2.64% in terms of mortality using brine shrimp lethality assay. Hydrogels showed antimicrobial properties against E. Coli using liquid diffusion method. Accumulative release of benzocaine was checked in phosphate buffer saline solution at 37 °C at pH 7.4 and observed that almost whole drug was released in 150 min. Hence, based on the aforementioned results, prepared hydrogels are proposed to be used for controlled drug release applications.



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sciforum-151118: Formulation of Lavender oil loaded Self-Microemulsifying Drug Delivery System for Psoriasis management

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Introduction

Psoriasis is a chronic, immune-mediated inflammatory skin disorder that demands effective and sustained therapeutic strategies. Conventional topical treatments often suffer from poor drug solubility, limited skin permeability, and systemic side effects. This study aimed to develop a novel Self-Microemulsifying Drug Delivery System (SMEDDS) incorporating lavender oil to enhance drug delivery and therapeutic efficacy for psoriasis management.

Methods

Comprehensive preformulation studies identified ethyl oleate as the oil phase, Tween 80 as the surfactant, and PEG 300 as the co-surfactant. A pseudo-ternary phase diagram guided the selection of an optimized oil-to-Smix ratio. The formulation was characterized for droplet size, zeta potential, and transmittance, and incorporated into cream bases with varying stearic acid concentrations. Analytical techniques including UV spectrophotometry and GC-MS validated the identity and purity of the drug and excipients. In vitro diffusion studies using Franz diffusion cells and cell line assays were conducted to assess drug release and biological activity. The HET-CAM assay was used to evaluate irritation potential.

Results

The optimized SMEDDS exhibited a droplet size of 147.3 nm, zeta potential of -26.1 mV, and transmittance of 92.57%, indicating a stable microemulsion. Among the cream formulations, the one with 10% stearic acid showed the best drug content and release profile. In vitro studies demonstrated sustained drug release over 24 hours, outperforming conventional formulations. Cell line studies revealed a 56% reduction in TNF- α expression and ROS reduction at 1 μ g/mL, indicating strong anti-inflammatory potential. The HET-CAM assay confirmed the formulation's non-irritating nature.

Conclusion

The developed lavender oil-loaded SMEDDS formulation significantly improved solubility, skin permeability, and controlled drug release, while demonstrating anti-inflammatory efficacy and safety. These findings support its potential as a novel, patient-friendly topical treatment for psoriasis.



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sciforum-151031: From CCD to ANN: A Hybrid Statistical-Computational Framework for Optimization of Doxylamine Succinate Orally Disintegrating Tablets

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INTRODUCTION

Orally disintegrating tablets (ODTs) are popular due to their rapid disintegration, improved patient compliance, and enhanced therapeutic efficacy. Designing ODTs requires careful optimization of formulation variables to achieve desired quality attributes. This study integrates Central Composite Design (CCD) and Artificial Neural Networks (ANN) to optimize Doxylamine Succinate ODTs using binder and superdisintegrant variables.

METHODS

CCD was used to design and develop directly compressed Doxylamine Succinate ODTs. Binder concentration (Povidone) and superdisintegrant (Croscopovidone) were the independent variables, with tablet friability, wetting time, and disintegration time as the dependent variables (responses). The compressed tablets were evaluated for all the responses. The dissolution studies were also performed in Hydrochloric Acid (0.01N). Response data were used to train the ANN-based model to optimize the formulation. ANN-based optimized formulation was assessed for drug release, and the release profiles of CCD and ANN-based optimized formulations were compared, using the f_2 test (similarity factor test).

RESULTS

All the CCD proposed formulations showed appropriate wetting time (10-12 seconds) with disintegration time ranging from 27-29 seconds and friability lower than 1%. All the formulations showed drug release above 80%. The highest drug release was observed with F7, which was considered the optimized formulation based on CCD results.

The selection of the optimal number of nodes influences the performance of the ANN model. The model for the current study was trained using the TanH values ranging from 3 to 10. The SSE and r^2 values were recorded at each node value. Node value 5 was the best activation node. The release profile of the ANN-optimized formulation was also assessed. The f_2 test demonstrated similarity between the two formulations.

CONCLUSION

The integration of ANN with CCD provides a robust, reliable, and multi-objective optimization platform for ODT development.



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sciforum-152276: From design to biological evaluation: AT11-liposomes boost imiquimod potential in tongue cancer cells

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Persistent Human Papillomavirus (HPV) infections can progress through a multistep carcinogenesis process, ultimately leading to invasive cancers. Imiquimod (IQ), a topical agent with antiviral and antitumoral properties, has shown promising outcomes in HPV-related pre-malignant lesions and even oral cancer case reports; however, its clinical application remains limited by poor solubility and low tissue selectivity. To overcome these challenges, nanoparticle-based systems such as liposomes, widely recognized for their safety and effectiveness in drug delivery, represent a promising strategy to enhance IQ therapy for oral cancers. Functionalization with targeting ligands may further enhance their selectivity. In this context, the nucleolin-binding aptamer AT11, which folds into a G-quadruplex structure, represents a valuable targeting moiety to promote selective drug accumulation in cancer cells.

Empty or IQ-loaded liposomes were prepared by the ethanol injection method and subsequently functionalized with AT11-TEG-Cholesteryl, yielding nanoparticles with hydrodynamic diameters of ~120-140 nm, and with %EE of ~83%. Their biological performance was assessed in squamous cell carcinoma of the tongue (UPCI-SCC-154) and non-malignant esophageal epithelial (Het1A) cells. Regarding their biological potential, AT11 IQ-associated liposomes allowed a selective delivery of IQ towards a tongue cancer cell line relative to the non-malignant cell line. Specifically, they induced a selective reduction of cell viability, proliferation and increased cell death. Additionally, they decreased the migration and invasion capacities of the cancer cells.

Overall, these findings highlight AT11-functionalized liposomes as a promising nanocarrier to improve the IQ selectivity and anticancer potential.

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sciforum-150520: Hybrid nanoparticles containing mesalazine for the treatment of inflammatory bowel disease: development, stability studies and *in vivo* fate

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Introduction: Zein and fucoidan are biomaterials useful to obtain hybrid nanoparticles to be orally administered and employed for the treatment of inflammatory bowel disease (IBD). Zein is stable in gastrointestinal fluids while fucoidan confers mucoadhesion and intrinsic anti-inflammatory activity to the nanosystems.

Methods: Nanoparticles were obtained by nanoprecipitation using zein and fucoidan at various weight ratios and they were employed to entrap mesalazine (5-ASA). The physico-chemical properties, entrapment efficiency and release rate of the active compound in simulated gastrointestinal fluids were evaluated by dynamic light scattering, FT-IR and spectrophotometric analyses, respectively. The muco-adhesive interactions were assessed monitoring their mean diameter and surface charge after incubation with porcine gastric mucin (0.1–0.5% w/v, 37 °C, up to 4 h). The antioxidant activity was investigated by the DPPH assay. Additional studies were performed in *Caenorhabditis elegans* in order to evaluate the *in vivo* fate of hybrid nanoparticles.

Results: Hybrid zein–fucoidan nanoparticles showed mean sizes of 100 nm, a narrow size distribution (PDI 0.2), a negative Zeta potential ($\zeta \approx -55$ mV) and an encapsulation efficiency of ~60% when 0.6 mg/mL of 5-ASA were used. They demonstrated to preserve the antioxidant activity of 5-ASA in simulated gastrointestinal fluid and the incubation with mucin confirmed the mucoadhesive properties of the nanosystems. *In vivo* studies in *Caenorhabditis elegans* showed a strong biocompatibility of the nanosystems, a useful intake and favorable effects on fat accumulation, oxidative stress and aging biomarkers.

Conclusions: Zein–fucoidan hybrid nanoparticles containing 5-ASA represent innovative nanomedicine to be employed for the treatment of IBD.



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sciforum-145036: Injectable Biodegradable Implantable Matrices For Prolonged Anti-VEGF Delivery: Toward Minimally Invasive Retinal Treatments

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Introduction

Diabetic retinopathy (DR) and age-related macular degeneration (AMD) are leading causes of vision loss, primarily driven by pathological angiogenesis mediated by vascular endothelial growth factor (VEGF). Sunitinib, a multi-targeted tyrosine kinase inhibitor, offers potent anti-angiogenic activity but is limited by systemic toxicity and rapid degradation. This research aimed to develop and evaluate biocompatible, biodegradable elastomeric implants for the sustained intraocular delivery of sunitinib, thereby reducing injection frequency, maintaining therapeutic drug levels, and improving ocular tolerability.

Methodology

Implants were formulated using poly(diols-co-tricarballoylate) elastomers via thermal crosslinking, incorporating sunitinib either through solvent casting or direct mixing. In vitro characterization included FTIR, DSC, XRD, drug release kinetics, and cytocompatibility on ARPE-19 cells. In vivo studies were conducted in rabbits, assessing ocular pharmacokinetics, fundoscopic examination, and histopathological analysis over a 42-day period following intravitreal implantation. Quantification of drug levels in vitreous humor and tissues was performed using validated LC-MS/MS.

Results

The elastomeric implants demonstrated amorphous drug dispersion, slow degradation, and pH-stable, diffusion-driven release extending up to 222 days. No burst effect was observed. Drug release followed Higuchi kinetics, with higher loading (1000 µg) resulting in increased release rates. Cytotoxicity studies revealed that controlled-release systems significantly reduced sunitinib-induced cell apoptosis and preserved proliferation in ARPE-19 cells. In vivo, all sunitinib implants were well tolerated with no significant vitreous hemorrhage or inflammation. Pharmacokinetic analysis confirmed sustained intraocular drug presence, with the highest levels seen in the 1000 µg implants.

Conclusion

This study successfully demonstrates the feasibility of using biodegradable elastomeric implants for long-term, controlled intraocular delivery of sunitinib. The system offers enhanced therapeutic duration, minimized dosing frequency, and improved safety compared to conventional injection-based therapies. These findings hold strong translational potential for treating neovascular retinal diseases such as DR and AMD, addressing the unmet clinical need for prolonged, cost-effective, and minimally invasive ocular drug delivery solutions.



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sciforum-151425: Injectable In-Situ Forming Thermoreversible Nanoemulgel of Lidocaine for Enhanced and Prolonged Anesthetic Action

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Background and Objectives:

Lidocaine hydrochloride (LD-HCl) is the most widely used local anesthetic in dentistry, commonly combined with epinephrine to prolong anesthesia and limit systemic absorption. However, its short duration of action, need for repeated injections, and bitter taste often reduce patient compliance and procedural efficiency. This study aimed to develop and evaluate an injectable in-situ forming nanoemulsion-based gel depot system of LD designed to provide sustained anesthetic activity.

Methods:

LD nanoemulsions were prepared by high-shear homogenization followed by probe sonication using Miglyol 812 N (oil phase), Tween 80 and soy lecithin (surfactant-co-surfactant), glycerin, and deionized water (aqueous phase). The optimized formulation (S1) was incorporated into a thermoreversible poloxamer solution to yield a nanoemulgel. The formulation was evaluated for particle size, distribution, zeta potential, morphology, pH, drug content, stability, rheology, injectability, and in vitro release. Analgesic efficacy was assessed in Wistar rats by tail-flick and paw withdrawal latency tests, while cardiovascular safety was monitored using non-invasive electrocardiography and blood pressure measurements.

Results:

The optimized nanoemulsion exhibited spherical morphology with a mean particle size of 206 nm, high negative zeta potential (-66.67 mV), and narrow distribution (PDI $\approx$ 0.40). The nanoemulgel demonstrated desirable thixotropic behavior, ensuring ease of injection. In vitro release studies showed sustained lidocaine release for 5 hours, following the Higuchi model. In vivo, the nanoemulgel significantly prolonged analgesia, lasting up to 150 minutes (2.5 h) compared with conventional LD-HCl injection (p 0.001). No adverse cardiovascular effects were observed.

Conclusions:

The developed LD-loaded in-situ nanoemulgel offers a promising and patient-friendly alternative for dental and minor surgical anesthesia. By extending anesthetic duration, it reduces the need for repeated injections, improves patient comfort, and enhances procedural efficiency.



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sciforum-148900: Intranasal delivery of combined nanostructured lipid carriers (NLC) formulations for enhanced migraine therapy

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Introduction: Migraine is a highly prevalent and disabling neurological disorder commonly managed through monotherapy, which often provides insufficient symptom relief due to its multifactorial pathophysiology. Combination therapy emerges as a promising alternative by targeting multiple mechanisms simultaneously. Nanostructured lipid carriers (NLC) offer additional advantages, namely improved drug stability and enhanced bioavailability. In this work, two NLC formulations were developed, encapsulating zolmitriptan and ibuprofen, respectively, with the aim of combining them for intranasal administration, enabling direct nose-to-brain delivery. This strategy is expected to enhance therapeutic efficacy while offering a non-invasive and patient-friendly approach for the management of acute migraine.

Methods: The Quality by Design (QbD) approach was applied to optimize the NLC formulations with respect to the Critical Quality Attributes (CQAs) of particle size (Z-Ave), polydispersity index (PDI), zeta potential (ZP) and encapsulation efficiency (EE).

Results: The optimized zolmitriptan- and ibuprofen-loaded NLC exhibited Z-Ave, PDI, ZP, and EE values of 62.373 ± 0.567 nm and 141.333 ± 2.301 nm; 0.209 ± 0.008 and 0.205 ± 0.004 ; -52.463 ± 0.264 mV and -14.323 ± 0.652 mV; and 74.231 ± 0.646 % and 84.376 ± 1.594 %, respectively. Both were subsequently combined into a final formulation, which displayed suitable physicochemical properties for intranasal delivery: Z-Ave of 188.850 ± 2.333 nm, PDI of 0.233 ± 0.007 , ZP of -16.297 ± 0.488 mV, osmolarity of 280 mOsm/kg, and pH of 6.06.

Conclusion: The QbD approach proved to be a valuable tool for optimizing both NLC formulations, resulting in suitable characteristics for nose-to-brain delivery. Future studies are needed to assess the cytotoxicity of the combined NLC formulation in nasal and neuronal cell lines, in order to evaluate its biocompatibility and safety for intranasal migraine therapy.



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sciforum-148142: Ivermectin Loaded Solid Lipid Nanoparticles for Ovarian Cancer Treatment: Development, Characterization and Enhanced Cytotoxic Activity

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Introduction: The ivermectin is a broad-spectrum antiparasitic drug from the avermectin family, has recently gained attention for its potential anticancer properties. This study focuses on the formulation development of ivermectin-loaded solid lipid nanoparticles (lv-SLNs) and evaluating release kinetics and nano-sized formulation effect in ovarian cancer cells.

Methods: The lv-SLNs were formulated using Box-Behnken experimental design and characterized in terms of physicochemical properties (particle size, zeta potential, polydispersity index, and entrapment efficiency), drug release profile, and release kinetics. The anticancer activity of lv-SLNs was assessed in OVCAR-3 cells and compared to ivermectin in suspension form (lv-SUSP).

Results: The lv-SLN formulation was characterized by particle size (154.5 ± 41.3 nm), polydispersity index (0.204 ± 0.02), zeta potential (-17.4 ± 3.93 mV), and entrapment efficiency ($81.34 \pm 5.67\%$) respectively. Release kinetics indicated that lv-SLNs act as a sustained release system and adhering to Higuchi kinetics ($r^2 = 0.981$). In-vitro cytotoxicity studies showed that lv-SLNs exhibits enhanced anti-cancer effect on OVCAR-3 cells than ivermectin suspension (2.1-fold).

Conclusion: Nano drug delivery systems offer advantages such as biocompatibility, enhancing drug's solubility, improving drug's bioavailability, and targeted drug delivery, which may help overcome drug resistance and improve treatment efficacy. This study highlights lv-SLNs as a promising nano-sized drug delivery system for ivermectin, and potentially enhancing its effectiveness in ovarian cancer therapy.



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sciforum-142458: Liposomes for potential delivery of *Aloe vera* waste antioxidants

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Aloe vera L. leaves possess bioactive principles, such as polyphenols, anthraglycosides, free anthraquinones, mono- and polysaccharides, polypeptides, terpenoids, sterols, chromones, lectins, fatty, amino and organic acids, enzymes, and saponins. *A. vera* waste (leaves without aloe gel) is also rich in amino acids, organic acids, flavonoids, anthraquinones, lipids, minerals, vitamins, carbohydrates, pigments, as well as volatile organic components. Hence, the aloe by-product is recognized as being of significant worth after the extraction of its bioactives and their potential implementation in food and cosmetic products. The encapsulation of the mentioned bioactive compounds can improve their stability, bioavailability, activity, and prolonged release in various formulations. Therefore, liposomes with aloe leaf waste extract were prepared using phospholipids and the pro-liposome technique, and their size, polydispersity index (PDI), and antioxidant potential before and after UV irradiation were examined using photon correlation spectroscopy and ABTS and DPPH assays, respectively. The vesicle size of aloe waste extract-loaded liposomal particles was 335.00 ± 20.55 nm (non-treated liposomes) and 326.63 ± 3.43 nm (after UV irradiation), whereas the PDI values were very high, 0.505 ± 0.056 and 0.712 ± 0.045 , respectively. The data mentioned above confirm the existence of nanoliposome vesicles in the non-uniform system. The anti-ABTS activity was 100.27 ± 2.08 μ mol Trolox equivalent (TE)/L (non-treated liposomes) and 103.11 ± 4.01 μ mol TE/L (after UV irradiation). The IC₅₀ value (the concentration of the sample required to scavenge 50% of free radicals) of non-treated liposomes with aloe waste extract was 59.77 ± 1.08 μ g/mL, while the IC₅₀ for the UV-irradiated sample was 57.81 ± 1.59 μ g/mL. Thus, UV irradiation did not cause changes in the size and antioxidant capacity of aloe waste extract-loaded liposomes, while the mentioned treatment caused a significant increase in the PDI value. Since UV irradiation did not cause a decrease in the antioxidant activity of the sample, it can be concluded that the liposomal membrane effectively protects sensitive aloe waste antioxidants from UV degradation.



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sciforum-152314: Multiple Emulsions for Anti-Inflammatory Treatment of Chemoradiotherapy-Induced Skin Damage

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Introduction: Oncological therapies (radiotherapy/chemotherapy) often impair the skin barrier, leading to erythema, dryness, and inflammation. These changes make conventional topical formulations unsafe, as they may provoke irritation or cause uncontrolled drug penetration, resulting in either toxic or sub-therapeutic exposure. Multiple water-in-oil-in-water (W/O/W) emulsions offer a promising solution, providing controlled release, drug stabilisation, and better tolerability for fragile, inflamed tissue. Emulsion complex structure (aqueous droplets within larger oil drops) enables modulation of drug transport across damaged skin. **Methods:** Sodium diclofenac was encapsulated in W/O/W emulsions. Emulsion characterisation included diclofenac encapsulation efficiency, droplet size, three-month stability, and rheological behaviour. Transdermal delivery was evaluated in Franz diffusion cells using synthetic membranes and skin models subjected to UV-irradiation or cytostatic-induced inflammation to simulate post-therapy conditions. Drug concentration was quantified spectroscopically. Fibroblast viability was assessed with PrestoBlue assay. **Results:** Emulsions exhibited high encapsulation efficiencies ($70.3 \pm 0.7\%$ - $95.8 \pm 0.7\%$), droplet diameters of 15.1 ± 0.5 - 22.5 ± 0.9 μm , less than 15% size variation during storage, and showed shear-thinning behaviour consistent with the Power law model (consistency indices: 0.363–0.480 $\text{Pa}\cdot\text{s}^n$; flow indices: 0.640–0.682; $R^2 > 0.99$). Damaged skin models displayed markedly increased and irregular permeability; conventional diclofenac formulations penetrated excessively and intensified irritation. In contrast, W/O/W emulsions provided modulated release, maintained therapeutic concentrations of drug. Fibroblasts exposed to UV/cytostatic damage showed >25% higher survival with diclofenac-loaded emulsions compared to standard solutions, indicating protective and regenerative potential. **Conclusions:** W/O/W emulsions represent a rational approach to transdermal delivery of anti-inflammatory drugs in oncology patients with impaired skin barrier. By ensuring controlled release and enhanced tolerability, they improve the safety of topical therapy.

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sciforum-151792: Nanoparticle and lipid nanocapsule formulations to enhance benznidazole dissolution: comparative evaluation and kinetic modeling

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Introduction: Benznidazole (BNZ), a poorly water-soluble drug, is the first-line treatment for Chagas disease; however, long treatment periods at high doses often cause adverse effects with insufficient efficacy in the chronic phase. This study aimed to design and compare benznidazole-loaded nanoparticles (NPs) and lipid nanocapsules (LNCs) with the pure drug, focusing on dissolution enhancement and kinetic modeling to support strategies for improving oral bioavailability.

Methods: LNCs were prepared by the phase inversion technique, yielding formulations with an average diameter of 50 nm, an encapsulation efficiency between 83–92%, and drug loading between 0.66–1.04%. NPs were obtained by the liquid anti-solvent precipitation process, also with diameters of approximately 50 nm. Both systems were evaluated and compared with the pure drug by in vitro release assays in simulated gastric medium at 37 °C. The experimental data were fitted to the Lumped-Gonzo model, which provided pharmaceutically relevant parameters and showed an excellent fit to the release profiles ($R^2 > 0.99$).

Results: The pure drug exhibited very limited dissolution, requiring more than 280 minutes to reach 20% release ($t_{20\%}$) and showing a mean dissolution time ($MDT_{20\%}$) close to 90 minutes. In contrast, LNCs doubled the initial release rate compared with BNZ, reduced $MDT_{20\%}$ to around 33 minutes, and increased dissolution efficiency (DE_{360min}) to 26.3%. NPs showed the most remarkable performance, achieving a very fast initial release rate of 1.5701 %/min and a maximum release of 89.2%.

Conclusions: Both formulations enhanced benznidazole dissolution compared with the pure drug, with LNCs showing a moderate but sustained effect and NPs achieving the most pronounced improvement. These findings highlight the potential of nanocarriers, particularly NPs, as promising platforms for improving BNZ oral bioavailability.



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sciforum-143077: Next-Gen vaccine analytics: Computational optimization of lipid nanoparticle mRNA delivery systems using machine learning

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This study presents a machine learning-driven framework to optimize critical quality attributes (CQAs) of mRNA-lipid nanoparticle (LNP) vaccines, addressing challenges in microfluidic manufacturing process efficiency and formulation stability. mRNA-LNP formulations ($n = 24$) were developed to evaluate the interplay of material attributes (ionizable lipids, phospholipids, PEGylated lipids), process parameters (flow rate ratio: 3–5; total flow rate: 12–20 mL/min), and lipid ratios (ionizable-to-cholesterol: 1.08–1.33; phospholipid-to-PEG: 3.76–6.67; N/P: 6–10) using I-optimal design of experiments (DOE). Key outcomes—including particle size (PS), polydispersity index (PDI), encapsulation efficiency (EE), and thermal stability—were analyzed using XGBoost/Bayesian optimization for microfluidic condition tuning (accuracy >94%) and a self-validated ensemble model (SVEM) for lipid mixture prediction (accuracy >97%). Results demonstrated that ionizable lipid selection significantly influenced LNP size: formulations with DOTAP achieved larger nanoparticles (94–96 nm) with high EE (95.5%), while MC3 produced smaller LNPs (51–57 nm) with reduced EE (79–85%). SVEM outperformed traditional models, with predicted PS (95–97 nm) closely matching experimental outcomes (94–96 nm). Furthermore, dual optimization of lipid ratios and process parameters enabled 96.6% encapsulated mRNA recovery and stabilized thermal profiles (heat trend cycle: -25°C to -10°C). Sucrose incorporation during lyophilization inhibited eutectic crystallization, maintaining PS within ± 2 nm post-freezing. This work highlights the first application of SVEM for simultaneous lipid/process optimization in mRNA-LNP production, offering a quality-by-design (QbD) approach to accelerate scalable, continuous manufacturing. The framework's >97% predictive accuracy supports rapid virtual screening of formulations, reducing experimental costs by 40%, and paves the way for robust, thermally stable vaccines tailored for diverse therapeutic applications.



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sciforum-126227: Optimization of the process of preparing microneedle patches based on natural polymer

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Introduction

Microneedle patches are modern systems for the transdermal delivery of active substances. One type of such systems comprises dissolvable patches based on natural polymers. A critical step in the preparation of these patches is to thoroughly fill the mold so as to obtain sharp tips of microneedles and remove all air bubbles. The aim of the study was to optimize the preparation process of dissolvable microneedle patches based on sodium hyaluronate.

Methods

For this purpose, 10 % w/w aqueous solutions of sodium hyaluronate were prepared using five different methods: (i) sonication, (ii) shaking, (iii) mechanical mixing, (iv) mechanical mixing combined with sonication, and (v) mechanical mixing combined with shaking. The resulting solutions were poured into silicone molds. In order to optimize the accurate filling of the mold and eliminate residual air bubbles, the molds with the solution were subjected to one of the following conditions: (i) no additional treatment, (ii) sonication, (iii) shaking, or (iv) three cycles of freezing and thawing.

Results

Preparation of the polymer solution using only sonication or a shaking was very time-consuming. Mechanical mixing alone or combined with shaking caused the solution to become aerated. However, mechanical mixing combined with sonication allowed the sodium hyaluronate to dissolve quickly and without aeration of the solution. The mold filled only by pouring the solution, or with using only ultrasounds or a shaker resulted in incomplete filling and the needles were not formed. On the contrary, three cycles of freezing and thawing allowed the mold to be completely filled and sharp needles were obtained.

Conclusions

Mechanical mixing combined with sonication was the most effective method for preparing a homogeneous, nonaerated polymer solution. The most efficient mold filling and sharp microneedle formation was achieved by applying three cycles of freezing and thawing to the filled molds.



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sciforum-151805: Predictive kinetic modeling of ciprofloxacin release from lipid-based nanocarriers for enhanced oral bioavailability

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Introduction: The development of efficient drug delivery systems remains a major challenge in pharmaceutical sciences. Nanomaterials, thanks to their exceptional properties, are fundamental to advancements in this field. Among them, lipid-based nanocarriers—such as solid lipid nanoparticles (SLN) and lipid nanocapsules (LNC)—stand out for their ability to encapsulate both hydrophilic and lipophilic drugs, improving solubility and stability, and enabling targeted or controlled release. Ciprofloxacin was used as a model drug in dissolution studies due to its well-documented properties. This study aimed to design and optimize lipid nanocarriers (SLN and LNC) for oral ciprofloxacin delivery, evaluating their stability and release profiles through predictive kinetic modeling to enhance bioavailability and support the rational development of nanomedicines.

Methods: SLN were synthesized using Gelucire 44/14, Span 80, and Tween 80, while LNC were prepared with Kolliphor, soybean lecithin, and Labrafac. Transmission electron microscopy confirmed that both nanocarriers exhibited spherical morphology with an approximate diameter of 50 nm.

Results: Encapsulation efficiencies were 97.9% and 98.0% for SLN and LNC, respectively. Stability studies over two months revealed that LNC remained stable at both 4°C and 25°C, whereas SLN experienced notable particle size changes after 7 days at 25°C. Release profiles in simulated gastric fluid were successfully fitted using the Lumped-Gonzo kinetic model, yielding high correlation coefficients ($R^2 = 0.9980$ and 0.9886 for LNC and SLN, respectively).

Conclusions: These results demonstrate that predictive kinetic modeling is a valuable strategy for guiding the rational design of stable and effective lipid-based nanocarriers to improve ciprofloxacin oral bioavailability.



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sciforum-152288: Quality by design (QbD) driven development of sinensetin embedded hydrogel for diabetic wound healing applications.

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Diabetic wounds represent one of the most serious complications of diabetes mellitus, often leading to delayed healing and increased risk of infection. Conventional therapies are limited in efficacy, which necessitates the development of novel therapeutic strategies. In this study, we aim to design and evaluate a sinensetin-loaded hydrogel formulation for the management of diabetic wounds, applying the principles of Quality by Design (QbD) to optimize its development. Sinensetin, a pentamethoxyflavone found in the leaves of *Orthosiphon aristatus* (Cat's whiskers) and citrus fruit peels, has been reported to possess strong antioxidant, anti-inflammatory, and antimicrobial properties, making it a promising candidate for wound healing applications. The hydrogel will be formulated and characterized through advanced techniques, including FESEM, FT-IR, XRD, DSC, TGA, viscosity, pH, spreadability, *in vitro* drug release, entrapment efficiency and texture analysis. *In vitro* studies will be performed to assess antioxidant, antimicrobial, and anti-inflammatory activities. For *in vivo* evaluation, diabetes will be induced in rats using a high-fat diet (HFD) combined with a low-dose STZ injection, followed by excision wound creation. Percentage wound contraction, re-epithelialization, collagen deposition, biochemical study and histopathological features will be studied alongside molecular assays of inflammatory cytokines and growth factors. This work is expected to provide scientific evidence for the wound healing efficacy of sinensetin hydrogel, highlighting its potential as a novel therapeutic approach for diabetic wound management.



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sciforum-151620: Research of polyethylenimine and anionic peptides as vehicles for plasmid DNA delivery *in vitro* and *in vivo*

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Introduction: Gene therapy holds immense therapeutic potential, but its efficacy relies on safe and efficient gene delivery systems. Non-viral vectors, such as polyethylenimine (PEI), offer advantages over viral methods, including lower immunogenicity and easier fabrication. The primary challenge of non-viral gene delivery vectors lies in their lower transfection efficiency compared to viral systems. This study investigates novel PEI-based ternary complexes utilizing anionic peptides to enhance plasmid DNA delivery by mitigating the significant cytotoxicity and non-specific interactions associated with cationic vectors.

Methods: We developed ternary polyelectrolyte complexes comprising plasmid DNA, PEI, and anionic, glutamate-rich peptides (E6p, cRGD-E6p, E6Hp, E6p0), which varied in their histidine content and the presence of an $\alpha\text{v}\beta 3$ integrin-targeting ligand (cRGD). Their transfection efficiency was evaluated *in vitro* using PANC-1 cells and *in vivo* via intramuscular injection in *m. quadriceps f.* in mice. Reporter genes (lacZ and GFP) were used to quantify efficiency of delivery through β -galactosidase assays and fluorescence microscopy.

Results: Optimal charge (Phosphorus/Nitrogen/Carboxyl) ratios for high transfection efficiency were identified. For the E6p0 peptide, the most effective DNA/PEI/peptide ratio was 1/16/2, while for E6p, cRGD-E6p, and E6Hp, it was 1/16/4. Reducing the injection volume to two-fold did not compromise transfection efficiency but minimized tissue damage *in vivo*. All formulations achieved statistically significant transfection levels compared to the control group. Peptides E6p0 and E6p showed the highest performance *in vivo*, evidenced by a greater number of GFP-positive muscle fibers.

Conclusion: The designed ternary complexes exhibit high efficacy for plasmid DNA delivery both *in vitro* and *in vivo*, highlighting their strong potential as versatile vectors for therapeutic gene delivery applications.



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sciforum-149959: Smart P407-based Thermogels Containing 5-ASA as Next Generation Rectal Formulations for the treatment of Inflammatory Bowel Diseases

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Introduction: Inflammatory bowel disease (IBD) is a chronic inflammatory disorder of the gastrointestinal tract that severely compromises quality of life. First-line therapy with 5-aminosalicylic acid (5-ASA) is limited by poor solubility, rapid absorption in the upper gut, and insufficient colonic delivery. Rectal formulations may overcome these issues, but conventional suppositories and enemas often reduce patient compliance.

Methods: Poloxamer 407 (P407)-based thermosensitive hydrogels were prepared using the cold method by dissolving the copolymer (20% w/w) in cold water and incorporating 5-ASA (0.1–0.5% w/w). The systems were characterized by rheological behavior, gelation temperature, mucoadhesive strength, injectability and spreadability. Drug release was evaluated at pH 5.0 and 7.4 by dialysis and membrane-less methods. Anti-inflammatory effects were tested in lipopolysaccharide-activated RAW264.7/Caco-2 co-cultures and in dextran sodium sulfate (DSS)-induced murine colitis model.

Results: The optimized P407-5-ASA hydrogel showed rapid gelation at physiological temperature, mucoadhesion, shear-thinning flow and easy syringeability, ensuring patient-friendly administration. 5-ASA showed prolonged release profiles even under acidic conditions. *In vitro* tests demonstrated that the formulation decreased both the macrophage infiltration and TNF- α secretion compared to free drug. Rhodamine-labelled gels demonstrated prolonged colon retention and P407-5-ASA markedly improved the therapeutic outcomes in DSS-treated mice with respect to commercial 5-ASA.

Conclusions: P407-based *in situ* hydrogels provide a high-performance, patient-acceptable platform for localized IBD therapy. They enhance 5-ASA efficacy and retention combining thermo-responsive gelation, mucoadhesion and sustained release while minimizing systemic exposure.

The obtained results support their potential as next-generation rectal formulations to improve the therapeutic outcomes and adherence in IBD patients.



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sciforum-149871: Targeting Neuroinflammation and Tau/APP Pathology via Intranasal Delivery of Azilsartan Medoxomil Nanoemulgel in AlCl_3 -induced Alzheimer's Dementia Model

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Background: Cognitive impairment and dementia have become a global burden, distressing millions of elderlies, accounting for progressive loss of neurons in the brain affecting higher multiple cortical centers, and impacting social life. The renin-angiotensin system and its receptors, widely distributed within the brain, offer potential to treat dementia via diminishing oxidative stress, neuronal inflammation, and increasing blood-brain barrier (BBB) integrity. The present study delves into the formulation and optimization of thermoresponsive azilsartan medoxomil (AZL-M) loaded *in situ* nanoemulgel for targeted nose-to-brain delivery to the brain due to low BBB permeability and validated through *in vivo* models.

Methods: A Box-Behnken design was used to optimize formulation parameters such as droplet size, gelation temperature, and drug release. The optimized nanoemulgel was characterized for physicochemical properties and evaluated for *ex-vivo* nasal mucosal toxicity, *in-vitro* cytotoxicity, and ROS reduction. *In-vivo* efficacy of intranasal application of the optimized formulation was assessed in an AlCl_3 -induced Alzheimer's model.

Results: Formulation-F20 showed optimal gelation at 33.4°C, pH-6.21, droplet size of 160nm, 60.4% drug release in 8h, high permeation, and flux, with confirmed safety and cell viability. TEER studies confirmed the integrity of RPMI-2650 monolayers, and while apparent permeability values of AZL-M solution and nanoemulgel were comparable, the nanoemulgel exhibited significantly higher cumulative permeation across the nasal epithelial barrier. *In-vivo* studies showed that nanoemulgel significantly improved cognitive performance and neuronal survival. At the molecular level, AZL-M treatment led to a marked reduction in brain inflammatory cytokines $\text{TNF-}\alpha$ and $\text{IL-1}\beta$, along with downregulation of Alzheimer's-specific markers including phosphorylated tau, amyloid precursor protein, and NF- κ B. Simultaneously, a significant upregulation of brain-derived neurotrophic factors indicated enhanced neurotrophic support and synaptic plasticity.

Conclusion: The intranasally delivered AZL-M-loaded nanoemulgel showed potential as a safe and effective therapy for Alzheimer's dementia by attenuating neuroinflammation and Alzheimer's pathology markers.



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Session 12. Biopharmaceutics, Pharmacokinetics and Pharmacodynamics

sciforum-146403: In silico evaluation of EGFR PROTACs' ADMET properties based on linker structure

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Proteolysis-targeting chimeras (PROTACs) are heterobifunctional molecules consisting of two linked substructures: protein-of-interest-binding ligand (POI ligand) and the E3 ubiquitin ligase-binding ligand. In this case, POI is the epidermal growth factor receptor (EGFR). EGFR is a transmembrane protein involved in cellular proliferation, angiogenesis, apoptosis and cancer metastasis in case of overexpression (particularly in lung cancer). Simultaneous binding of the PROTAC to both the EGFR and the E3 ligase leads to the ubiquitylation of the EGFR, thus marking it for degradation via the ubiquitin proteasome system. First EGFR PROTACs were developed in 2001, but all early synthetic PROTACs exhibited similar issues- high molecular weight and hooking effect, leading to poor ADMET properties of ligands.

To address those issues on a broad scale, scientists investigated whether PROTAC linker structure impacts biodegradation efficacy and PROTAC pharmacokinetics. However, the impact of linker structure on PROTACs' DMPK properties is still not well understood. In this research we employed literature research to understand the current practices in EGFR PROTAC synthesis with improved ADMET properties. Based on theoretical findings, we have designed EGFR PROTAC structures employing one of the following linker modifications: i) linker length; ii) linker rigidity; iii) number of hydrogen donors in linker; iv) number of introduced heteroatoms. All compounds were tested in silico for the evaluation of their ADMET properties, using freely available online ADMET Tools: SwissADME, ADMETlab 2.0, pkCSM6, ADMET-AI, Simulations Plus ADMET Predictor.

Obtained results show that the AI tools have a higher precision in predicting ADMET properties of drugs not conforming to the rule of 5. The increase in linker length for EGFR PROTACs leads to improved bioavailability and decreased carcinogenicity, and higher linker rigidity causes increased plasma protein binding. Higher number of HBD leads to decreased oral acute toxicity, and the higher number of heteroatoms causes a decrease in hERG blocking.



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sciforum-152175: Patient digital twin for peptide muscle relaxant activity control

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Physiologically based pharmacokinetic (PBPK) modeling serves as an important tool in drug development and personalized therapy. It enables the integration of individual patient physiological characteristics to predict drug distribution across tissues, which is particularly relevant for chronic diseases, impaired liver and kidney function, as well as for off-label application scenarios or evaluation of new compounds.

This work presents an interactive PBPK model that describes drug distribution across 13 major body compartments: blood, liver, kidneys, lungs, heart, muscle and adipose tissue, brain, bones, gut, spleen, skin, and other tissues. The model is based on systems of ordinary differential equations (ODEs). Key pharmacokinetic parameters are incorporated in the calculations: some are determined experimentally (e.g., logP, unbound drug fraction, hepatic clearance), while others are obtained from literature sources (e.g., pKa).

A distinctive feature of this development is its complete implementation within the open-source R environment using the deSolve package for numerical integration of equations. This approach ensures full transparency, reproducibility of results, and easy integration with other statistical and bioinformatic tools. The model is integrated with an intuitive Shiny/plotly web interface, allowing flexible adjustment of administration route, organ clearance, dosing regimen, and frequency.

As a case study, simulations were performed for azemiopsin - a peptide neurotoxin with muscle relaxant properties. The model demonstrated pronounced drug accumulation in muscle tissue with rapid clearance from systemic circulation. An additional module simulated antibody-antigen interaction, which is considered and modeled within the framework of the drug-drug interaction (DDI) concept. This demonstrates the platform's capability to analyze complex pharmacokinetic scenarios and various dosing regimens.

The PBPK model shows high flexibility and practical value. It can be used for planning preclinical studies, optimizing experimental protocols, refining ADME profiles, and predicting individual body responses to drugs, thereby creating a foundation for personalized pharmacotherapy.



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sciforum-148719: Mechanistic Insights into Drug Release and In Vitro Pharmacokinetics – Vildagliptin, Fast Disintegrating Tablets with Superdisintegrants

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Objective: Fast-disintegrating tablets (FDTs) have gained significant attention in pharmaceutical research due to their ability to disintegrate rapidly in the oral cavity without the need for water. This improves patient compliance, particularly in pediatric and geriatric populations. The present study formulated and evaluated FDTs using various Superdisintegrants to enhance drug dissolution and bioavailability.

Methods: The tablets were prepared by direct compression, employing sodium starch glycolate, croscarmellose sodium, and crospovidone as Superdisintegrants at different concentrations. A comprehensive preformulation study assessed the powder blend's flow properties, including bulk density, tapped density, Carr's index, Hausner's ratio, and angle of repose, to ensure uniformity and ease of compression. Post-compression evaluation of the tablets involved weight variation, hardness, friability, thickness, disintegration time, and content uniformity to determine their physicochemical properties.

Results: The results revealed that all formulations exhibited satisfactory pre-compression and post-compression characteristics. However, formulation F6 (containing 15 mg of crospovidone) had the shortest disintegration time (3 min 10 s) and the highest drug release (99.56% in 30 minutes) compared to the other formulations. F6 also showed the lowest friability (0.11%), indicating excellent mechanical strength; its content uniformity was highest (99.81%), ensuring uniform drug distribution in each tablet. In vitro dissolution studies demonstrated that drug release significantly improved with increasing superdisintegrant concentration, with crospovidone being the most effective among those tested. Kinetic analysis indicated that the formulations followed zero-order release kinetics and fit the Higuchi diffusion model, suggesting a diffusion-controlled release mechanism. Based on these findings, the optimized formulation (F6) was identified as the most promising due to its rapid disintegration, enhanced dissolution rate, and superior mechanical properties.

Conclusion: This study highlights the significance of selecting an appropriate superdisintegrant to achieve optimal tablet performance. The use of crospovidone at 15 mg was the most effective in producing FDTs with excellent pharmaceutical characteristics. Formulation F6 is recommended for further in vivo evaluation and potential commercialization, offering significant advantages in improving drug bioavailability and patient compliance.



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sciforum-152321: Pharmacokinetics and inhibitory activities of UPLC-detected compounds of *Voacanga africana* roots on acetylcholinesterase and monoamine oxidase B: Potential drug candidates for neurological disorders

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Introduction: *Voacanga africana* is a widely used medicinal plant in Africa for the treatment of several diseases, including mental disorders. This study investigated the ADME properties and inhibitory potential of compounds detected in the roots of the plant on acetylcholinesterase (AChE) and monoamine oxidase B (MAO-B), targets implicated in neurological disorders.

Methods: The roots of *V. africana* were extracted with 80% methanol, after which the extract was subjected to UPLC-ESI-MS/MS in negative mode. Known compounds were docked against AChE and MAO-B obtained from the Protein Data Bank (PDB ID: 4EY7 and 4A7A, respectively), using AutoDock. Drug likeness and ADME prediction were achieved using SwissADME and vNN-ADMET online servers, respectively. Rivastigmine and Rosiglitazone were used as the standard inhibitors of AChE and MAO-B, respectively.

Results: Some of the compounds had higher binding affinities against AChE and MAO-B compared to the standards, which had binding affinities of -8.0 and -9.8 kcal/mol, respectively. The top five compounds inhibited both targets with binding affinities of -12.4 to -9.6 kcal/mol for AChE and -12.1 to -10.2 kcal/mol for MAO-B. They include tsangibeilin B, rel-, Elisabatin B, Pinocembrin 7-[4-(1-hydroxyethyl)phenyl] ether, Hedyotol C and obochalcolactone. Tsangibeilin B, rel- had the highest binding affinity for both targets. It exhibits desirable drug-likeness properties, acts as a P-glycoprotein inhibitor and substrate, permeates the blood-brain barrier, is stable with respect to the human liver microsomal stability assay, and does not inhibit cytochrome P450 enzymes.

Conclusion: The top-scored compounds, especially tsangibeilin B, rel- therefore, pose as potent inhibitors of AChE and MAO-B, demonstrating their potential in neurological disorders..



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sciforum-150910: Targeting Genetic Mutations in Chronic Myeloid Leukemia: Insights into MUC3A Mutation and Regulatory Alterations in MIR5195 for Personalized Therapeutic Approaches

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Chronic Myeloid Leukemia (CML) progression from chronic phase (CP) to advanced stages such as accelerated phase (AP) or blast crisis (BC) remains a major clinical challenge, particularly due to limited early detection biomarkers. In this study, we investigate the genetic mutations driving CML progression, focusing on the MUC3A gene and the downstream regulatory region of the MIR5195 gene. We identified a novel missense mutation, P258S, in MUC3A that is exclusively present in AP/BC-CML patients. Structural and physicochemical analyses revealed that the P258S mutation alters protein stability, increasing flexibility in some regions and stabilizing others, which may affect its molecular interactions. Molecular dynamics simulations and docking studies showed enhanced binding affinity of MUC3A P258S with several therapeutic agents, particularly Capmatinib, suggesting potential clinical applications in treating CML. Additionally, mutations in the MIR5195 regulatory region were found to disrupt transcription factor binding, leading to changes in gene expression patterns. MEME and TOMTOM motif analysis revealed the loss of key motifs and the emergence of new ones in the mutant sequences, indicating a shift in the transcriptional regulation landscape. These findings suggest that these mutations may influence the expression of genes involved in CML progression. This study highlights the potential of MUC3A and MIR5195 as biomarkers for CML progression and therapeutic targets for personalized treatment strategies. The identified P258S mutation in MUC3A opens new avenues for targeted therapies, while the regulatory alterations in MIR5195 offer insights into gene expression reprogramming in CML's advanced stages.



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sciforum-152109: Theoretical-experimental study of metronidazole solvatochromism

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Metronidazole (MTZ) is a nitroimidazole antimicrobial widely used to treat various anaerobic bacteria and protozoa infections. MTZ is a small lipophilic molecule with an oral bioavailability higher than 90 %. An analytical theoretical-experimental solvatochromic study of MTZ that improves its pharmacokinetics understanding has not been done yet. To this research, twelve pure solvents: two non-polar, six polar aprotic, four polar protic, and buffer pH 7.4 were chosen. The spectrophotometric study was performed with 1×10^{-5} M MTZ solutions. The TD DFT B3LYP and CAMB3LYP with the PCM in its IEFPCM formalism and the 6-311+G(d,p) basis set were used to obtain the MTZ UV-Vis theoretical spectra. Kamlet and Taft, Catalán and Laurence multiparametric equations were utilized to analyze the effect of the solvent environment on MTZ. These analyses exhibit positive solvatochromism. The mayor Kamlet and Taft's relative contribution was from non-specific π interactions, accounting for 65 %. Catalán and Laurence equations showed that these non-specific contributions were mostly due to polarizability and dispersion forces (65 % SP and 72 % DI). While hydrogen-bond specific interactions were much less relevant: 35 % β , 16 % SB, and 20 % β_1 . All calculated maximum wavelengths, which correspond to the electronic transitions of the second singlet states for MTZ, were from HOMO to LUMO. These results show that polarizability rises significantly in polar solvents, reflecting enhanced electron cloud distortion, besides the high polarity of MTZ. Greater polarizability typically correlates with increased permeability through biological membranes, as the molecule can interact more effectively with the lipid environment and adapt to changes in polarity between the aqueous medium and the lipid bilayer membrane. This evidence could explain the easy penetration of MTZ into the microorganism cell by passive diffusion.



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