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2nd Edition
2026

Conference

The 2nd International Electronic Conference on Medicinal Chemistry and Pharmaceutics

1–30 November 2026 | online



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The 2nd International Electronic Conference on Medicinal Chemistry and Pharmaceutics

1–30 November 2026 | Online

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Welcome from the Chair

Dear Colleagues,

We cordially invite you to join us at **the 2nd International Electronic Conference on Medicinal Chemistry and Pharmaceutics (ECMC-P 2026),** sponsored by MDPI's open access journals *Pharmaceuticals* and *Pharmaceutics*.

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-P2026. 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 *Pharmaceuticals* and *Pharmaceutics*, which includes the following general topics:

S1. Invited Lectures;

S2. General;

S3. New Small Molecules as Drug Candidates;

S4. Natural Products and Biopharmaceuticals;

S5. Novel Methodologies and AI;

S6. New Modalities in Drug Discovery;

S7. Radiopharmaceuticals;

S8. Nanomedicine and Nanotechnology;

S9. Formulation, Drug Delivery, and Controlled Release;

S10. Biopharmaceutics, Disposition, Pharmacokinetics and Pharmacodynamics.

Researchers are invited to provide a short abstract (250 words maximum without figures and references) online, through this link from now until **17 September 2026.**

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 2026 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 2026**.

All participants will be invited to submit a full paper describing their work. The papers will be peer-reviewed and, upon acceptance, published in the conference's 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, *Pharmaceuticals* and *Pharmaceutics.*

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,



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pharmaceuticals

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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: 5.7 (2025); 5-Year Impact Factor: 5.5 (2025)



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 pharmaceutics 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: 6.9 (2025); 5-Year Impact Factor: 6.7 (2025)

Invited Speakers



Dr. André Ferreira Moreira

BRIDGES - Biotechnology Research, Innovation, and Design of Health Products, Polytechnic of Guarda, Guarda, Portugal; RISE-Health, Departamento de Ciências Médicas, Faculdade de Ciências da Saúde, Universidade da Beira Interior, Covilhã, Portugal



Prof. Dr. Elena Sánchez López

Department of Pharmacy and Pharmaceutical Technology and Physical Chemistry, Faculty of Pharmacy, University of Barcelona, Spain



Dr. Sónia Alexandra Pereira Miguel

BRIDGES - Biotechnology Research, Innovation and Design for Health Products, Polytechnic University of Guarda



Prof. Animesh Ghosh

Solid State Pharmaceutics Research Laboratory, Department of Pharmaceutical Sciences and Technology Birla Institute of Technology, Jharkhand, India



Dr. Dinesh Kumar

Department of Pharmaceutical Engineering & Technology, Indian Institute of Technology, Banaras Hindu University, Varanasi, India



Prof. Ana Catarina Silva

FP-BHS (Biomedical and Health Sciences Research Unit), FP-I3ID (Instituto de Investigação, Inovação e Desenvolvimento), Faculty of Health Sciences, University Fernando Pessoa, Porto, Portugal; UCIBIO, Laboratory of Pharmaceutical Technology, Faculty of Pharmacy, University of Porto, Porto, Portugal; Associate Laboratory i4HB Institute for Health and Bioeconomy, Faculty of Pharmacy, University of Porto, Porto, Portugal



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Prof. Dr. Tin Wui Wong

Non-Destructive Biomedical and Pharmaceutical Research Centre, Smart Manufacturing Research Institute, Universiti Teknologi MARA, Selangor, Malaysia



Dr. Zyta M Ziora

Institute for Molecular Bioscience, University of Queensland, Brisbane, Australia



Dr. Magdalena Paczkowska-Walendowska

Department of Pharmacognosy and Biomaterials, Poznan University of Medical Sciences, Poznan, Poland



Dr. Donatella Ambroselli

Department of Science and Bio-Technology, Campus Bio-Medico University of Rome, Rome, Italy



Dr. Martina Bortolami

Department of Basic and Applied Sciences for Engineering (SBAI), Sapienza University of Rome, Rome, Italy

Session 1. Invited Lectures

Sciforum-211462: From ethnobotanical evidence to natural drugs: investigation of *Commiphora* species from Socotra as sources of bioactive compounds

Martina Bortolami [1,*], Chiara Toniolo [1], Fabio Sciubba [1, 2], Adriano Patriarca [3], Ilaria Serafini [1], Dario La Montagna [1], Stefania Garzoli [4], Petr Maděra [5], Kay Van Damme [5], Fabio Attorre [1], Luca Santi [1] and Daniela De Vita [1]

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In the Socotra Archipelago (Yemen), a natural UNESCO World Heritage Site known for its unique biodiversity and high rate of endemism, there are five resin-producing plants of the genus *Commiphora* or myrrh trees: *C. kua* (R.Br. ex Royle) Vollesen, *C. ornifolia* (Balf.f.) J.B.Gillett, *C. planifrons* Engl., *C. parvifolia* Engl., and C*. socotrana* Engl. From an ethnobotanical point of view, these plants are very important for their traditional uses including medical purposes and as sources of incense.

Despite this, these species are currently poorly studied with regards to their bioactive compounds. Therefore, the present research investigated the phytochemical composition of the resins produced by the *Commiphora* species from Socotra. For this purpose, the collection and the export of the resin samples were authorized by the Environment Protection Authority (EPA) of the Republic of Yemen, which oversees the Socotra Archipelago.

Headspace solid-phase microextraction coupled with gas chromatography–mass spectrometry (HS-SPME/GC-MS) was carried out for the analysis of the volatile fractions of the resins from each of the five *Commiphora* species of Socotra. Based on the obtained results, the studied resins are mainly rich in monoterpenes and sesquiterpenes, showing different trends in accordance with the ecology of the areas where the samples were collected.

From the non-volatile fraction of the resin of *C. ornifolia,* (+)-yangambin was isolated. This furofuran lignan, known for its vasorelaxant, cardiovascular, anti-tumour and antileishmanial activities, has previously been reported in *Commiphora* genus only in *C. wightii* (Arn.) Bhandari.

The analysis of the hydrolyzed polysaccharide fraction of *C. ornifolia* by high-performance thin-layer chromatography (HPTLC) and nuclear magnetic resonance (NMR) revealed the presence of arabinose, rhamnose, galactose, and galacturonic acid.

Overall, these findings provide a first phytochemical rational for the traditional uses of *Commiphora* species from Socotra and suggest that these plants might generate other bioactive molecules of pharmaceutical value.

Future studies will aim to isolate additional compounds from the *Commiphora* species of Socotra and to evaluate their potential biological activities useful for pharmaceutical applications.



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Sciforum-212284: Carbohydrates Meet Sulfur: From Stereodivergent Synthesis to Sulforaphane-Inspired Medicinal Chemistry

Inmaculada Fernandez [1,*], Victoria Valdivia Giménez [1], Rocío Recio [2], Luis Alberto Prieto Ramírez [2], Li Tao [2] and NORA KHIAR FERNÁNDEZ [1]

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Carbohydrates are abundant renewable chiral building blocks whose structural diversity, low cost, and well-established chemistry make them attractive tools for asymmetric synthesis and medicinal chemistry. Our work combines carbohydrate-derived stereochemical information with the distinctive reactivity and biological relevance of sulfur-containing compounds.

A key synthetic platform is the diacetone-D-glucose (DAG) methodology, which provides stereodivergent access to both configurations of sulfinates and, subsequently, to a broad range of enantiopure sulfoxides. Beyond their applications as chiral auxiliaries and ligands in asymmetric catalysis, these compounds have enabled the development of structurally diverse bioactive molecules.

Sulforaphane, (*R*)-1-isothiocyanato-4-(methylsulfinyl)butane, is a naturally occurring multitarget sulfoxide with pleiotropic biological effects, including activation of the NRF2 pathway and modulation of several cancer-related signaling mechanisms such as STAT3. It was therefore selected as a lead structure for medicinal-chemistry optimization. Different families of analogues were designed to improve biological activity, selectivity, stability, solubility, and synthetic accessibility. Structure–activity studies identified derivatives with enhanced NRF2 activation and selective cytotoxicity in cancer models. Bioisosteric replacement of the sulfinyl group led to simpler achiral candidates, including phosphorus-containing derivatives, while carbohydrate-based *N*- and S-glycosides were also developed as glycomimetic analogues with NRF2-activating and selective antiproliferative activity.

Overall, this work illustrates the dual role of carbohydrates as renewable sources of chirality and as scaffolds for molecular design, connecting stereoselective sulfur chemistry with the discovery and optimization of new bioactive compounds.

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Author contributions: Conceptualization, Inmaculada Fernandez; Methodology, Luis Alberto Prieto Ramírez, Li Tao and NORA KHIAR FERNÁNDEZ; Validation, Luis Alberto Prieto Ramírez, Li Tao and NORA KHIAR FERNÁNDEZ; Formal analysis, Luis Alberto Prieto Ramírez, Li Tao and NORA KHIAR FERNÁNDEZ; Investigation, Luis Alberto Prieto Ramírez, Li Tao and NORA KHIAR FERNÁNDEZ; Data curation, Luis Alberto Prieto Ramírez, Li Tao and NORA KHIAR FERNÁNDEZ; Supervision, Inmaculada Fernandez, Victoria Valdivia Giménez and Rocío Recio; Project administration, Inmaculada Fernandez, Victoria Valdivia Giménez and Rocío Recio; Funding acquisition, Inmaculada Fernandez;

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Sciforum-212520: Development of gold-based nanomaterials for biomedical applications.

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Gold-based nanomaterials have emerged as versatile platforms in nanomedicine due to their tunable optical properties, biocompatibility, and ease of surface functionalization. This presentation summarizes a series of studies focused on the design, synthesis, and biological evaluation of gold nanorods developed for combined chemo-photothermal therapy of cancer.

The production of gold nanorods can be optimized so that the nanoparticles exhibit strong near-infrared absorption, which, coupled with efficient light-to-heat conversion, enables localized hyperthermia (ΔT of 30°C) that can be harnessed to sensitize or kill cancer cells. Additionally, gold nanorods can simultaneously act as carriers for chemotherapeutic agents, enabling combinatorial and synergistic therapeutic approaches. To improve biological performance, these AuNRs were coated with polymers (such as PEOZ, PEI, and HA) to increase colloidal stability and circulation time, functionalized with targeting ligands to enhance cellular selectivity, or even camouflaged with red blood cell-derived membranes to confer immune evasion and biomimetic properties. Together, these strategies aimed to improve tumor accumulation and therapeutic efficacy while reducing off-target toxicity, demonstrating the potential of combined chemo-photothermal therapeutic approaches.

Altogether, these works illustrate the versatility of gold-based nanomaterials, in particular nanorods, and showcase them as multifunctional platforms for cancer therapy, underscoring the importance of rational design and surface engineering in advancing their clinical translation.



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Sciforum-213611: Natural Products for Advanced Wound Care

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Wound healing is a complex and dynamic biological process requiring the coordinated interaction of cells, extracellular matrix components and signalling molecules. The development of advanced wound dressings has therefore moved beyond simple wound protection towards multifunctional systems capable of supporting different stages of the healing process. In this context, natural products have attracted increasing interest due to their structural diversity and range of biological properties, including antioxidant, antimicrobial and regenerative activities.

This work provides an overview of the role of natural products in wound healing and their incorporation into advanced wound dressing systems. Different types of natural derived materials will be discussed, including biopolymers and bioactive compounds. Particular emphasis will be given to their application in different wound dressing, such as hydrogels, porous sponges and electrospun membranes.

Finally, current challenges and future perspectives in the development of natural product-based wound dressings will be discussed, highlighting the potential of combining natural bioactive compounds with advanced biomaterial technologies to develop more effective and multifunctional approaches to wound management.



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Sciforum-215391: Beyond the Scaffold: Engineering Smart Biomaterials for Regenerative Dentistry

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Regenerative dentistry requires advanced biomaterials capable of addressing multiple clinical challenges, including microbial infections, inflammation, and impaired tissue healing. Beyond providing structural support, modern biomaterials should combine controlled drug delivery with biological activity and properties tailored to specific clinical applications.

This presentation highlights the pharmaceutical design of multifunctional biomaterials for regenerative dentistry, focusing on baicalein-loaded chitosan sponges as a promising platform for local therapeutic applications. Baicalein, a naturally occurring flavonoid derived from Scutellaria baicalensis, exhibits antioxidant, anti-inflammatory, and antimicrobial properties. Its incorporation into chitosan-based matrices offers opportunities to combine these biological activities with the favorable properties of a biodegradable polymer.

A systematic formulation approach was employed to investigate the influence of chitosan molecular weight and concentration on sponge morphology, mechanical performance, drug release, mucoadhesion, and biological activity. Structural characterization demonstrated that formulation parameters significantly affected pore architecture and polymer interactions. Mechanical studies revealed the possibility of balancing elasticity and stiffness, while drug release experiments confirmed that polymer characteristics could be used to modulate release profiles. Biological evaluations demonstrated biocompatibility, antimicrobial potential, and favorable cellular responses, including support for cell attachment and migration.

Importantly, preclinical assessments using anatomical models and simulated surgical procedures highlighted the relevance of material adaptability, handling, and interactions with the biological environment.

These findings demonstrate that multifunctionality can be achieved through rational pharmaceutical design. By integrating structural, mechanical, pharmaceutical, and biological properties, a single biomaterial platform can be tailored to different therapeutic needs. Ultimately, successful translation of regenerative biomaterials requires moving beyond conventional scaffolds toward clinically oriented systems designed to address specific challenges in dental tissue repair.

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Author contributions: Conceptualization, Magdalena Paczkowska-Walendowska and Judyta Cielecka-Piontek; Methodology, Magdalena Paczkowska-Walendowska; Formal analysis, Magdalena Paczkowska-Walendowska; Investigation, Magdalena Paczkowska-Walendowska; Writing - original draft, Magdalena Paczkowska-Walendowska; Writing - review and editing, Judyta Cielecka-Piontek; Project administration, Magdalena Paczkowska-Walendowska; Funding acquisition, Magdalena Paczkowska-Walendowska;



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Sciforum-215512: Exploring Coprocessing Techniques to Improve the Materials Attributes of Active Pharmaceutical Ingredients

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Active pharmaceutical ingredients (APIs) frequently exhibit poor manufacturability despite acceptable pharmacological performance because crystal morphology, particle attributes, surface properties, and solid-state characteristics strongly influence powder processing and dosage-form performance. This work explored coprocessing strategies to engineer API material attributes and improve processability, with emphasis on ethambutol dihydrochloride (ETB) and voriconazole (VRZ).

ETB, a highly hydrophilic antitubercular drug, exhibits high-aspect-ratio crystals that are associated with poor flowability, hygroscopicity, and tabletability. A quasi-emulsion solvent diffusion (QESD) approach was investigated using hydroxypropyl methylcellulose (HPMC) grades E5, E15, and E50 to generate spherical agglomerates. Particle size, morphology, solid-state properties, powder flow, compressibility, tabletability, compactability, surface characteristics, dissolution, and intrinsic dissolution were systematically evaluated. Coprocessing transformed the challenging crystal morphology into more processable agglomerated particles and demonstrated improved powder-handling and compaction characteristics.

For DPI applications, coprecipitation of crystalline VRZ with HPMCAS polymers was investigated using controlled high-shear mixing and solvent–antisolvent processing. Solid-state characterization by differential scanning calorimetry, powder X-ray diffraction, and polarized light microscopy confirmed conversion of crystalline VRZ to amorphous solid dispersions. The resulting particles exhibited reduced size, improved flow properties, lower contact angle, and increased surface free energy, indicating enhanced wettability and dispersion. In vitro dissolution studies demonstrated substantially faster drug release, with a characteristic spring–parachute profile.

Overall, the findings demonstrate that API coprocessing can simultaneously engineer particle morphology, solid-state structure, surface properties, and bulk powder behavior. These approaches provide a versatile platform for improving API manufacturability, tablet performance, and dry-powder inhalation formulation, while potentially reducing reliance on conventional granulation and milling processes and improving process robustness.

Author contributions: Conceptualization, Dinesh Kumar; Methodology, Dinesh Kumar; Software, Dinesh Kumar; Validation, Dinesh Kumar; Formal analysis, Dinesh Kumar; Investigation, Dinesh Kumar; Visualization, Dinesh Kumar; Supervision, Dinesh Kumar;



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Sciforum-215590: From officinal plants to functional ingredients: phytochemical profiling, bioactivity and applications as food supplements

Donatella Ambroselli [1,*], Fabrizio Masciulli [2], Annalisa Chiavaroli [2], ALAIN MUSELLI [3], Laura Dugo [4], Luisa Mannina [5] and Cinzia Ingallina [6]

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Officinal plants represent rich reservoirs of bioactive secondary metabolites; however, their chemical composition varies significantly according to species, plant organ, and pedoclimatic conditions, presenting challenges for their standardization as food supplements and functional ingredients. To address this, an integrated metabolomic strategy was developed, combining complementary analytical platforms (NMR, HPLC-PDA, GC-MS), multivariate statistics, and cell/ex vivo bioassays to correlate phytochemical profiles with neuroprotective activities.

In the first case study, NMR-based metabolomics compared burdock (*Arctium lappa* L.), dandelion (*Taraxacum officinale*), and lemon balm (*Melissa officinalis*) across lowland spontaneous, mountain spontaneous, and organic cultivation ecotypes, revealing species as the primary driver of metabolic variation, with secondary, species-dependent ecotype effects. In the second case study, HPLC-PDA profiling demonstrated that mountain dandelion leaves contained the highest levels of chicoric and caftaric acids; these extracts preserved hypothalamic cell viability under oxidative stress and, in ex vivo LPS-treated mouse brain tissues, downregulated pro-inflammatory markers (TNF-α, NOS-2) while increasing neurotrophic BDNF expression. In the third case study, wild *Melissa officinalis* subsp. *altissima* from Corsica was characterized by GC-MS and NMR, revealing a sesquiterpene-rich essential oil, an (E)-β-ocimene-dominated headspace, and a polyphenol profile rich in rosmarinic, chlorogenic, and caftaric acids. These extracts suppressed TNF-α, NOS-2, IL-6, and acetylcholinesterase (AChE) expression in LPS- and β-amyloid-stimulated tissues.

Overall, environmental factors and plant organs shape the phytochemistry and bioactivity of officinal plants, establishing standardized dandelion and lemon balm extracts as promising functional candidates for brain health, pending further *in vivo* validation. These species may support the nutraceutical, cosmeceutical, and pharmaceutical industries.

Author contributions: Conceptualization, Donatella Ambroselli; Methodology, Donatella Ambroselli; Validation, Donatella Ambroselli; Formal analysis, Donatella Ambroselli; Investigation, Donatella Ambroselli; Data curation, Donatella Ambroselli; Writing - original draft, Donatella Ambroselli; Writing - review and editing, Donatella Ambroselli; Visualization, Donatella Ambroselli;

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Sciforum-215649: Lipid Nanoparticles for Cutaneous Formulations: From Formulation Development to Quality by Design and Scale-Up

Ana Catarina Silva *

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Lipid nanoparticles, particularly solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC), have attracted considerable interest as versatile platforms for the development of innovative cutaneous formulations. Their ability to incorporate and protect molecules, modulate their release, and improve formulation performance makes them promising systems for both pharmaceutical and cosmetic applications.

This presentation provides an overview of the fundamental principles of SLN and NLC, including their main characteristics and potential advantages for cutaneous applications. The main laboratory-scale approaches used for the preparation of aqueous lipid nanoparticle dispersions and semisolid formulations are presented. Selected examples of cutaneous applications are discussed, highlighting the potential of these systems to enhance the performance of pharmaceutical and cosmetic formulations.

Particular attention is given to the integration of Quality by Design (QbD) principles into lipid nanoparticle development. The identification of critical quality attributes (CQAs), critical material attributes (CMAs) and critical process parameters (CPPs) is discussed as a strategy to support formulation and process understanding, optimisation and reproducibility. The challenges associated with the scale-up of lipid-based nanocarriers are also addressed, with particular emphasis on the impact of changes in equipment and process conditions on nanoparticle characteristics and product quality.



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Sciforum-216935: A mechanistic elucidation behind the change in solubility and permeability of pharmaceutical cocrystals

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Pharmaceutical cocrystallization has been explored as a promising strategy to improve drug physicochemical properties. However, rational design of cocrystals with optimal desired properties remains challenging. In this study, we investigated the mechanism underlying the negligible solubility and permeability improvement of Acetazolamide (ACZ) cocrystals with highly soluble and lipophilic coformers, 4-hydroxybenzoic acid, salicylamide, and 4,4'-bipyridine. Lattice energy calculations showed that strong lattice stability limited solubility improvements, while solution-state ^{1}H NMR confirmed similar molecular states between cocrystals and physical mixtures, explaining the lack of solubility and dissolution improvement. Caco-2 permeability studies of cocrystals revealed no significant enhancement in ACZ permeability, consistent with the *in silico* molecular dynamics simulations showing unchanged stability of the ACZ-efflux transporter complex in the presence of coformers. These findings underscore the limits of conventional coformer selection and highlight the need for predictive tools. Based on the results, we propose an integrated model to predict cocrystal properties pre-synthesis and reduce trial-and-error.

Author contributions: Conceptualization, Animesh Ghosh; Methodology, Animesh Ghosh; Formal analysis, Animesh Ghosh; Resources, Animesh Ghosh; Data curation, Animesh Ghosh; Writing - review and editing, Animesh Ghosh; Supervision, Animesh Ghosh; Project administration, Animesh Ghosh; Funding acquisition, Animesh Ghosh;



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Session 2. General

Sciforum-209057: Evolution-guided systems biology reveals host therapeutic vulnerabilities associated with the SARS-CoV-2 primase complex

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The SARS-CoV-2 primase complex, composed of nonstructural proteins 7 and 8 (nsp7–nsp8), is indispensable for viral RNA replication and represents one of the most evolutionarily constrained components of the viral replication machinery. We hypothesized that structural features preserved despite global viral evolution may underpin conserved host-pathogen interactions that can be exploited therapeutically. To investigate this, we integrated population-scale mutation surveillance, structural bioinformatics, affinity-purification mass spectrometry, quantitative proteomics, structural modelling, and functional validation to characterize the biological consequences of nsp7–nsp8 expression. Evolutionary analyses of globally circulating SARS-CoV-2 variants identified mutation-tolerant regions alongside structurally constrained interfaces predicted to be essential for primase complex stability and function, supporting the conservation of critical molecular features despite continuous viral diversification. Guided by these findings, we systematically investigated the host proteomic landscape associated with nsp7–nsp8 expression and identified coordinated remodeling of host molecular networks and cellular programs, supported by complementary structural analyses. Functional validation further demonstrated that these systems-level perturbations reveal a previously unrecognized host therapeutic vulnerability, where pharmacological modulation of a prioritized host pathway produced potent antiviral activity and enhanced efficacy when combined with an approved antiviral agent in a SARS-CoV-2 replicon model. Collectively, this study establishes an evolution-informed systems biology framework linking structural conservation of an essential viral replication complex with host-cell reprogramming and therapeutic intervention, providing a strategy for identifying host-directed antiviral targets that remain resilient to viral genetic variation.

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Sciforum-209865: DNA-protective activity of selected compounds in the development of HDAC4-targeting PROTACs for spinal muscular atrophy

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Spinal muscular atrophy (SMA) is an inherited neuromuscular disorder characterised by insufficient levels of the survival motor neuron (SMN) protein and progressive loss of motor neuron function. The disease is primarily caused by alterations in the *SMN1* gene, while the paralogous *SMN2* gene provides a limited source of functional SMN protein due to its predominant alternative splicing pattern. Consequently, reduced SMN availability compromises motor neuron maintenance and ultimately leads to progressive muscle weakness and atrophy. Although disease-modifying therapies have substantially improved the clinical management of SMA, the identification and characterization of additional therapeutic approaches remain important research objectives. In that sense, targeted degradation of HDAC4 using PROTAC molecules to switch off the HDAC4-atrogin 1-Murf-1 atrophy-associated transcriptional program could be a rational palliative care approach. However, selective HDAC4 degradation could trigger oxidative DNA damage in skeletal muscle by modulating maladaptive GADD45A/myogenin-associated stress signalling, mitochondrial-redox homeostasis, ROS burden, and DNA-damage response pathways involved in genome maintenance. Therefore, four PROTACs developed as anti-SMA agents, namely **TG-49**, **PJ-594**, **PJ-653**, and **PJ-655**, confirmed as HDAC4 degraders in Jurkat cells, were evaluated *in vitro* at concentrations of 25, 50, 100, 200, and 400 μg/mL for their protective potential against oxidative DNA damage. DNA-protective activity was assessed using assays based on hydroxyl- and peroxyl-radical-induced DNA damage. All tested compounds exhibited DNA-protective activity against both hydroxyl- and peroxyl-radical-induced oxidative damage across the entire tested concentration range. These findings demonstrate the DNA-protective potential of the investigated compounds and provide additional *in vitro* evidence supporting their further biological characterization.

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Sciforum-210156: Photoinactivation of different growth forms of *Candida albicans* mediated by porphyrin-polyethylenimine conjugates

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Candida albicans is a major cause of superficial candidiasis. Although antifungal therapies are widely available, their effectiveness can be compromised by biofilm formation and the emergence of drug resistance. Thus, photodynamic inactivation has emerged as a promising alternative approach for the treatment of fungal infections. In this work, two porphyrin-polyethylenimine conjugates were evaluated as photosensitizers to photoinactivate *Candida albicans*. Planktonic yeast suspensions (1×10^6 CFU/mL) in phosphate-buffered saline (PBS) were treated with the conjugates (1.0 and 2.5 μM) for 30 min in the dark and subsequently irradiated with white light. Photoinactivation increased with both photosensitizer concentration and light fluence. Complete elimination of planktonic *C. albicans* was achieved with 2.5 μM $TPPF_{10}$TFA-PEI after 30 min of irradiation, whereas TPP_{10}CBZ-PEI produced a 2 log reduction in cell survival under the same conditions. Experiments using reactive oxygen species scavengers confirmed that singlet molecular oxygen was the predominant reactive species involved in the photoinactivation process for both conjugates. $TPPF_{10}$TFA-PEI was also effective against *C. albicans* pseudohyphae in PBS, with the reduction in viability increasing with both the conjugate concentration and irradiation time. Finally, the ability of the conjugates to inhibit *C. albicans* biofilm development on poly(vinyl chloride) (PVC) discs was evaluated by incorporating the photosensitizers during the biofilm proliferation phase. Under these conditions, $TPPF_{10}$TFA-PEI at 5.0 μM produced a 2 log reduction in biofilm viability, whereas TPP_{10}CBZ-PEI achieved a 1 log reduction. Therefore, these results demonstrate that $TPPF_{10}$TFA-PEI is an effective photosensitizing conjugate for the photoinactivation of *C. albicans* under planktonic, pseudohyphal, and biofilm growth conditions, highlighting its potential as a phototherapeutic agent for the treatment of fungal infections.

Author contributions: Conceptualization, María Gabriela Alvarez, Paula Verónica Cordero Gabrielli, Lucila Luna, Milena Belén Boarini, María Elisa Milanesio and Edgardo Néstor Durantini; Methodology, María Gabriela Alvarez, Paula Verónica Cordero Gabrielli, Lucila Luna, Milena Belén Boarini, María Elisa Milanesio and Edgardo Néstor Durantini; Validation, María Gabriela Alvarez, Paula Verónica Cordero Gabrielli, Lucila Luna, Milena Belén Boarini, María Elisa Milanesio and Edgardo Néstor Durantini; Formal analysis, María Gabriela Alvarez, Paula Verónica Cordero Gabrielli, Lucila Luna, Milena Belén Boarini, María Elisa Milanesio and Edgardo Néstor Durantini; Investigation, María Gabriela Alvarez, Paula Verónica Cordero Gabrielli, Lucila Luna, Milena Belén Boarini and María Elisa Milanesio; Data curation, María Gabriela Alvarez, Paula Verónica Cordero Gabrielli, Lucila Luna, Milena Belén Boarini and Edgardo Néstor Durantini; Writing - original draft, María Gabriela Alvarez; Writing - review and editing, Edgardo Néstor Durantini; Visualization, María Gabriela Alvarez, Paula Verónica Cordero Gabrielli, Lucila Luna, Milena Belén Boarini, María Elisa Milanesio and Edgardo Néstor Durantini; Supervision, María Gabriela Alvarez, María Elisa Milanesio and Edgardo Néstor Durantini; Project administration, Edgardo Néstor Durantini; Funding acquisition, Edgardo Néstor Durantini;



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Sciforum-210536: Zinc(II) Complexation Enhances the Antidiabetic and Antioxidant Properties of Cinnamic Acid

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This study aimed to develop a novel zinc–cinnamic acid nutraceutical with enhanced and multimodal antidiabetic and antioxidant properties. A Zn(II) acetate complex of cinnamic acid was synthesized and characterized using FT-IR and ^1H NMR spectroscopy. Cytotoxicity was evaluated. Antioxidant activity was assessed using DPPH and ABTS radical-scavenging and Fe^3+-reducing assays. Antiglycation activity and inhibitory effects against α-glucosidase and α-amylase were also evaluated. The insulin-mimetic activity of the complex was assessed based on glucose uptake in differentiated L6 myotubes. Molecular docking was subsequently performed against GLUT4 and protein kinase B (PKB/Akt). FT-IR and ^1H NMR analyses indicated that Zn(II) coordinated with cinnamic acid through an oxygen-based coordination mode, forming a complex containing two cinnamic acid ligands. Zn(II) complexation significantly enhanced the antiglycation activity of cinnamic acid ($p < 0.05$), reducing its IC_50 from 29.3 to 13.9 μM (approximately 2.1-fold enhancement). Notably, complexation conferred pronounced glucose uptake activity (EC_50 = 31 μM) and α-glucosidase inhibitory activity (IC_50 = 59.4 μM) on cinnamic acid, with the complex exhibiting approximately 162- and 2.1-fold greater activities, respectively, than the parent compound ($p < 0.05$). Molecular docking further demonstrated stronger interactions of the Zn(II)–cinnamic acid complex with GLUT4 and PKB/Akt than with cinnamic acid alone. Importantly, the complex exhibited no marked cytotoxicity at the concentrations evaluated. The findings demonstrate a structure–activity relationship in which Zn(II) complexation substantially enhances the antidiabetic and antiglycation properties of cinnamic acid. The resulting complex exhibited multifunctional pharmacological activities, including enhanced glucose uptake, α-glucosidase inhibition and antiglycation activity, while maintaining a favourable cytotoxicity profile. These findings support further investigation of the Zn(II)–cinnamic acid complex as a potential nutraceutical candidate for glycaemic management and the prevention of diabetes-associated glycation-related complications.

Author contributions: Conceptualization, Chika Ifeanyi Chukwuma; Methodology, Chika Ifeanyi Chukwuma; Formal analysis, Chika Ifeanyi Chukwuma; Resources, Chika Ifeanyi Chukwuma; Writing - original draft, Chika Ifeanyi Chukwuma; Funding acquisition, Chika Ifeanyi Chukwuma;



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Sciforum-210778: Concentration and time-dependent effects of Fe_3O_4 nanoparticles on acteoside and echinacoside production in *Scrophularia striata* Boiss. cell suspension cultures

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Scrophularia striata Boiss. is a valuable medicinal plant and a rich source of biologically active specialized metabolites, particularly phenylethanoid glycosides (PhGs), including acteoside and echinacoside, which possess considerable pharmaceutical and industrial potential. Plant cell culture provides a controlled and sustainable platform for the production of these valuable metabolites. However, their relatively low accumulation under in vitro conditions necessitates the development of effective elicitation strategies. In this study, the concentration- and time-dependent effects of iron oxide nanoparticles (Fe_3O_4 NPs) as a novel abiotic elicitor on specialized metabolite production in *S. striata* cell suspension cultures were investigated. Treatment with Fe_3O_4 NPs at concentrations ranging from 5 to 100 mg L^{-1} induced a nonlinear response in the accumulation of acteoside and echinacoside, with the strongest overall response observed at 5 mg L^{-1}. Notably, echinacoside accumulation increased more than sevenfold compared with the control at this concentration, suggesting a hormetic response and a high sensitivity of the PhG biosynthetic pathway to nanoparticle dosage. Based on these results, 5 mg L^{-1} was selected to investigate temporal responses over 1–96 h. Fe_3O_4 NPs induced a sequential and time-dependent response characterized by controlled oxidative signaling, coordinated antioxidant defense, enhanced activities of phenylalanine ammonia-lyase and tyrosine ammonia-lyase, and activation of the shikimate and phenylpropanoid pathways. These responses were associated with increased accumulation of PhGs. Both acteoside and echinacoside reached their maximum levels at 24 h, followed by a gradual decline and subsequent stabilization, indicating metabolic readjustment after the peak defense response. Overall, the findings demonstrate that Fe_3O_4 NPs can reprogram specialized metabolism in *S. striata* in a concentration- and time-dependent manner. The combination of a low nanoparticle concentration and an appropriate exposure period, particularly 24 h, represents a promising strategy for enhancing the production of valuable bioactive metabolites in *S. striata* cell suspension cultures.

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Sciforum-210839: Reduction of glycosylimines: Synthetic strategies and carbonic anhydrase inhibitory activity

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Glycomimetics have emerged as a class of compounds of significant pharmacological interest, as they have proven useful for the development of selective enzyme inhibitors. In our group, glycosylimines capable of selectively inhibiting carbonic anhydrase (CA) IX, an isoform overexpressed in tumor tissues, have been previously reported.[1] Glycosylimines were obtained from D-glucosamine and substituted aromatic aldehydes under basic conditions. In this work, their two complementary reduction strategies, homogeneous and heterogeneous, were investigated and compared, followed by evaluation of the inhibitory activity of the resulting compounds against CA.

Homogeneous reduction with sodium cyanoborohydride ($NaBH_3CN$) in the presence of acetic acid (AcOH) afforded the corresponding glycosylamines in yields ranging from 18 to 60%, depending on the aromatic substituent. In contrast, sodium borohydride ($NaBH_4$) provided low yields ($<$15%) under the conditions evaluated.

Heterogeneous catalytic hydrogenation was also explored under mild conditions (30 °C, 4 atm H_2) using Ni/C, Pd/C, Pt/C, Pd-Fe/C, and Pt/SiO_2 catalysts. Most systems showed low activity or promoted substrate degradation. Among them, 1% Pt/SiO_2 achieved approximately 35% substrate conversion after 24h, although the desired product was isolated in low yield. These results indicate that the homogeneous reduction strategy was more efficient in terms of isolated yield.

The glycosylamines obtained by $NaBH_3CN$ reduction were evaluated against human carbonic anhydrase isoforms I, II, IX, and XII. The p-hydroxybenzaldehyde derived and vanillin derived compounds showed inhibitory activity toward CA IX and CA XII, with Ki values ranging from 5.3 to 20.8 μM. These results support glycosylamine derivatives as promising scaffolds for the design of selective inhibitors targeting tumor-associated carbonic anhydrase isoforms.

1. Vásquez, I. R., Riafrecha, L. E., Martínez Heredia, L., Echeverría, G. A., Piro, O. E., Lavecchia, M. J., Supuran, C. T., & Colinas, P. A. (**2025**). Journal of Molecular Structure, *1321*, 139778.

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Sciforum-210844: Enhanced skin delivery of triamcinolone acetonide using invasome-based formulations

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Transdermal delivery of triamcinolone acetonide was investigated using an invasome based formulation designed to enhance skin penetration and drug deposition. The formulation incorporated phospholipids, ethanol and selected terpenes to improve drug permeation across the stratum corneum. Ethanol and terpenes are expected to increase membrane fluidity and facilitate penetration into deeper skin layers. Invasomes were prepared using a mechanical dispersion approach, in which the drug and terpene were dissolved in ethanol containing phospholipids, followed by vortexing and sonication. The resulting dispersion was hydrated with phosphate buffer (pH 7.4) to obtain the final formulation. Compared with conventional liposomal systems, the developed invasome formulation showed enhanced skin penetration and drug deposition, while limiting systemic exposure. The formulation promoted drug localization within the epidermal and dermal layers, demonstrating its potential for site specific topical delivery of triamcinolone acetonide.



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Sciforum-210853: Flavonoid-Rich Profiles across Different Populations of Six Iranian *Achillea* Species

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Achillea L. (Asteraceae) is a medicinally important genus with a long history of use in traditional and folk medicine for the treatment of various ailments. The genus is characterized by a diverse and rich phytochemical composition, particularly phenolic compounds and flavonoids, which have been widely investigated for their antioxidant, anti-inflammatory, and antimicrobial properties. Among these constituents, luteolin, apigenin, and their derivatives are of particular interest because of their documented pharmacological properties. The present study aimed to characterize individual phenolic and flavonoid compounds in six Iranian *Achillea* species and their populations using high-performance liquid chromatography (HPLC). Considerable interspecific and population-level variation was observed in the accumulation of individual metabolites. For example, luteolin 6,8-di-C-glucoside was found to reach its highest content (14.55 mg g^{-1} dry weight) in *A. kellalensis*, while vicenin-2, an apigenin C-glycoside, exhibited 7.09 mg g^{-1} dry weight in *A. wilhelmsii*. Several *A. wilhelmsii* populations showed particularly high levels of apigenin-derived flavonoids, including vicenin-2, vitexin, and apigenin-7-O-glucoside. In contrast, compounds such as luteolin, quercetin, and kaempferol exhibited varied distribution patterns among the evaluated species. The observed diversity in flavonoid profiles underscores the potential of Iranian *Achillea* as a source of pharmacologically relevant compounds. Consequently, the chemically enriched species and populations identified may serve as promising plant material for targeted compound isolation, bioactivity-guided screening, and further pharmacological and pharmaceutical research.



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Sciforum-210867: PepSMILES: SMILES Generator for Chemically Modified and Cyclized Peptides

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Chemically modified peptides are promising therapeutic scaffolds, but their database annotations and sequential labeling or adding metadata to raw data, so a machine learning model can learn from it remains difficult. Many peptides consist of features like non-proteinogenic residues, terminal derivatization, macrocyclization, and covalent links between chains. Chemical structure annotations of such modified peptides are only partly covered by existing sequence-to-structure tools.

We developed a Python application PepSMILES[1] that constructs atom-resolved molecular graphs from structured peptide records and exports stereochemical SMILES, V2000 MOL files, and two-dimensional images. The application currently includes more than 650 unusual-amino-acid blocks, together with 370 curated N- and C-terminal modifications. It supports up to 50 intrachain annotations found in the current DBAASP export and nine interchain annotations, including disulfide, amide, ester, thioether, carbon–carbon, heterocyclic, and multibridge closures. Assembly is metadata-driven: each residue and terminal template identifies the atoms involved in peptide or cross-link formation and any leaving groups, while chemistry-specific rules apply the required bond changes for each intra- or interchain modification. When applied at database scale, the workflow returned SMILES for 25,243 of 25,306 eligible DBAASP[2] records.

Applications like p2smi[3], cyclicpeptide[4], and PepLink[5], none reports this same combination of unusual-residue coverage, terminal derivatization, chemically diverse cyclization, and covalent multimer assembly.

By reducing manual structure drawing and taking advantage of reusable chemical rules, the application can shorten dataset preparation, improve structural consistency, and allow experimentally described peptides to be compared directly with small molecules in established drug-discovery pipelines.

This approach makes chemically complex peptides accessible to cheminformatics, QSAR, virtual-screening, and machine-learning workflows.

1. https://dbaasp-dev.ibrsp.org/tools?page=smiles-generator2. https://dbaasp.org/home3. https://github.com/AaronFeller/p2smi4. https://github.com/dfwlab/cyclicpeptide5. https://github.com/DragonDescentZerotsu/PepLink

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Sciforum-210921: Comparing Balb/c 3T3, HaCaT and 1BR.3.G for in vitro phototoxicity assessment: a preliminary study

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Phototoxicity testing is an important component of the safety assessment of chemicals and cosmetic and pharmaceutical ingredients. The BALB/c 3T3 NRU phototoxicity test is an established in vitro method for identifying phototoxic substances. The development of human-derived models may provide complementary and potentially more human-relevant approaches for phototoxicity assessment. This study aimed to compare the phototoxic responses of HaCaT and 1BR.3.G cells with the established cell model. Cells were exposed to different concentrations of chlorpromazine in the absence or presence of UVA irradiation (4 J/cm^2, Actinic BL UVA 15W/10 FAM/10X25BOX emitting at 350–370 nm region, 365 nm peak), following the principles of OECD TG 432. Photo-Irritation Factor (PIF) was determined using the NRU and MTT assays under irradiated and non-irradiated conditions. NRU and MTT values obtained were 26.1 ± 6.0 and 25.4 ± 3.1 for HaCaT, and 52.4 ± 28.7 and 28.4 ± 8.2 for 1BR.3.G classifying chlorpromazine as phototoxic. In the case of BALB/c 3T3 a substantial loss of viability in irradiated controls was already observed at low passages (P3–P5), shortly after cell acquisition, suggesting that extensive passaging was unlikely to account for the observed response. Collagen coating and reducing the UVA dose did not provide sufficient viability for reliable phototoxicity testing. Although HaCaT and 1BR.3.G have shown good response with CPZ further studies with a broader range of positive and negative reference chemicals are needed to assess their predictive capacity and applicability. Moreover, comparison with the BALB/c 3T3 model would be desirable.

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Sciforum-210932: Synthesis of a Trifluoromethyl-Substituted Thiophene Chalcone: A Spectroscopic Study

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Chalcone derivatives have attracted considerable interest in modern chemical research owing to their versatile molecular structures and diverse properties. In the present study, a (E)-1-(thiophen-2-yl)-3-[4-(trifluoromethyl)phenyl]prop-2-en-1-on was synthesized through condensation under basic conditions. The synthesized compound was investigated using UV–Visible, FTIR and NMR spectroscopic techniques to establish its structural features. The spectroscopic studies provide information on the characteristic functional groups, conjugated system and electronic properties of the synthesized compound, supporting the formation of the desired chalcone framework. The incorporation of both a thiophene moiety and a trifluoromethyl-substituted aromatic group provides an interesting structural modification within the chalcone system. The study highlights a simple synthetic approach towards a substituted chalcone and its spectroscopic investigation, providing a foundation for further exploration of its chemical properties and potential applications in biological field and corrosion studies.

Author contributions: Methodology, Divya N Shetty; Supervision, Divya N Shetty; Project administration, Divya N Shetty;



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Sciforum-210950: The effect of hydration on the fluorescent properties of protonated and deprotonated ribonucleotides and their constituents

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Our previous studies have demonstrated the antiviral activity of protonated 5′-ribonucleotides. To elucidate the molecular mechanisms of their biological action, it is important to determine the physicochemical properties of these compounds in an aqueous environment. It is known that hydration significantly influences the electronic states and fluorescence characteristics of nucleotides; however, the comparative characteristics of protonated ribonucleotide forms and their salts have not been sufficiently studied.

The aim of the study was to investigate the effect of hydration on the fluorescence characteristics of protonated 5′-ribonucleotides and their disodium salts. Three-dimensional excitation–fluorescence spectra were recorded in the dry state and in aqueous solution using a HORIBA FluoroMax-4P+ spectrofluorometer.

It was shown that hydration induced changes in the fluorescence spectra of the studied compounds in different ways, with the exception of protonated UMP. A significant enhancement of fluorescence was observed for protonated purine ribonucleotides. In the case of AMP, hydration was accompanied by a shift in the fluorescence maximum of 21 nm and an eightfold increase in intensity. For $AMPNa_2$, the corresponding changes were 25 nm and a 1.3-fold increase. For protonated GMP, a spectral shift of 55 nm and a 25-fold increase in intensity were observed. At the same time, two bands appeared in the spectrum of $GMPNa_2$ upon hydration. For CMP and $CMPNa_2$, shifts were 5 and 92 nm, respectively. Meanwhile, protonated UMP showed no response to hydration, whereas the fluorescence intensity of its sodium salt increased approximately threefold.

Hydration affects the fluorescence properties of protonated ribonucleotides and their disodium salts differently. The particularly pronounced effect observed for protonated AMP and GMP indicates the significant influence of the aqueous environment on their electronic-energy characteristics. These differences must be taken into account when investigating the interaction of ribonucleotides with biological targets and development of new medicines.

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Sciforum-210956: Proof-of-Concept Evaluation of the Diffuse Reflectance Kinetic Method for the Analysis of Biological Preparations in Turbid Media

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INTRODUCTION. The analysis of biological preparations in turbid media is challenging due to residual turbidity, multiple light scattering, and heterogeneous optical properties, which may complicate protein determination in complex adjuvanted formulations. Diffuse reflectance kinetics (DRK), based on monitoring the temporal dynamics of diffusely reflected light from sequential speckle images, offers a potential approach for characterizing turbid samples without prior clarification. **AIM.** To evaluate, as a proof-of-concept study, the applicability of DRK for protein-related analysis in turbid biological preparations, including concentration-dependent responses, matrix effects, calibration, and repeatability. **MATERIALS AND METHODS.** Bovine serum albumin (BSA) was analyzed at concentrations of 60, 120, 180, 240, and 360 μg mL^{-1} in a squalene-containing, TBS-based emulsion as a model of adjuvanted vaccine formulations. Ten DRK descriptors (d1, d2, d3, sd1, sd2, sd3, r1, r2, r3, and R) were calculated from sequential speckle images and evaluated relative to a BSA-free blank matrix using fold-change analysis. The most consistent descriptor (d2) was selected for exploratory linear calibration, and within-day repeatability was assessed at 180 μg mL^{-1} (n=6). For comparison with DRK, protein concentration was determined using the Pierce BCA Protein Assay Kit in homogeneous antigen-containing samples prior to squalene adjuvant addition. Measurements were performed at a nominal protein concentration of 180 μg mL^{-1} (90 μg per 0.5 mL dose). **RESULTS.** The d2 descriptor showed the most consistent monotonic concentration-dependent response, with linear calibration demonstrating a strong correlation with BSA concentration ($r = 0.9971$; $R^2 = 0.9942$). Within-day repeatability was favorable (CV = 1.13%). To further assess the applicability of DRK to VLP preparations, BCA and DRK results were compared, yielding comparable mean concentrations of 179.43 and 179.14 μg mL^{-1}, respectively, with low variability (CV = 0.44% and 1.31%, respectively). **CONCLUSION.** The findings support the feasibility of the DRK method for protein-related analysis in turbid biological preparations and justify further validation using matrix-matched calibration and multiple recovery levels. The close agreement between the mean values supports the feasibility of DRK for comparative monitoring of protein response in the investigated adjuvanted emulsion system.



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Sciforum-211027: Phytochemical Characterization and In-Silico Prediction of Molecular Interactions of *Cissus populnea* Guill. & Perr. Stem Constituents: Relevance to Male Reproductive Health

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Cissus populnea Guill. & Perr. is widely used in ethnomedicine for the management of reproductive disorders; however, its phytochemical composition and potential molecular interactions underlying its biological activity remain incompletely characterized. This study investigated the phytochemical constituents, functional group composition, and predicted molecular interactions of bioactive compounds from the ethanol and ethyl acetate fractions of *Cissus populnea* Guill. & Perr. stem using spectroscopic, chromatographic, and computational approaches. Fourier-transform infrared (FTIR) spectroscopy revealed functional groups consistent with hydroxyl, carbonyl, and aromatic-containing compounds, including phenolic and flavonoid constituents. High-performance liquid chromatography (HPLC) profiling identified thirteen phytochemical constituents, including caffeic acid, ferulic acid, sinapic acid, diphenyl ether, vanillic acid, quercetin, zeaxanthin, trolox, phenyl ether salicylic acid, nicotine, phenol, and theobromine. Molecular docking analysis was subsequently performed to predict the potential interactions of the identified compounds with sex hormone-binding globulin (SHBG), a protein involved in the regulation of circulating sex steroid bioavailability. The docking analysis revealed varying predicted binding affinities, with quercetin (-9.8 kcal/mol) and trolox (-9.3 kcal/mol) showing the most favorable docking scores. Predicted interactions involved hydrogen bonding, hydrophobic contacts, and π–π interactions within the SHBG binding pocket. **These computational findings suggest that some phytochemicals present in** *Cissus populnea* Guill. & Perr. **may interact favorably with SHBG and provide hypotheses for further biochemical investigation. However, the predicted interactions were not experimentally validated in the present study.**



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Sciforum-211088: Development and Characterization of a High-Fat High-Sucrose Dietary Model for Experimental Hepatic Injury in Wistar Rats

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Background:

Excessive consumption of dietary fat and simple sugars is associated with dyslipidemia, hepatic lipid accumulation, oxidative stress and chronic inflammation, contributing to metabolic liver disease. A standardized dietary model is important for investigating diet-associated hepatic injury in preclinical research.

Objective:

This study aimed to formulate and characterize a high-fat high-sucrose (HFHS) diet and evaluate its potential to induce metabolic and hepatic alterations in Wistar rats.

Methods:

An HFHS diet pellets was formulated using selected nutritional ingredients in defined proportions and evaluated for physical and nutritional characteristics. The formulation exhibited hardness of 10.91 ± 0.28 kg/cm^2 and friability of 0.80 ± 0.05%. Twelve male Wistar rats were divided into normal control (n=6) and disease control (n=6) groups. The disease group received the HFHS diet for 8 weeks. Body and liver weights, liver index, lipid profile, hepatic enzymes, oxidative stress markers, inflammatory mediators and hepatic triglycerides were assessed. Liver histopathology was also performed.

Results:

HFHS-fed rats showed increased body weight, liver weight/liver index, total cholesterol, triglycerides, LDL-C, ALT, AST and ALP, with decreased HDL-C. MDA/TBARS and oxidative stress increased, whereas SOD, catalase and GSH decreased. TNF-α, IL-6 and MCP-1 levels and hepatic triglyceride accumulation were increased. Histopathology revealed hepatic steatosis, hepatocellular ballooning, inflammatory infiltration, sinusoidal dilatation, vascular congestion and focal hepatocellular necrosis.

Conclusion:

The formulated HFHS diet produced dyslipidemic, oxidative, inflammatory and histopathological alterations after 8 weeks, demonstrating its potential as a reproducible preclinical model of diet-associated hepatic injury.

Author contributions: Methodology, Vaishnavi Tushar Mahajan; Formal analysis, Vaishnavi Tushar Mahajan; Investigation, Pavan Balasaheb Udavant ; Writing - original draft, Vaishnavi Tushar Mahajan; Writing - review and editing, Vaishnavi Tushar Mahajan; Visualization, Vaishnavi Tushar Mahajan; Supervision, Pavan Balasaheb Udavant ; Project administration, Vaishnavi Tushar Mahajan;



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Sciforum-211114: “Development and Characterization of a High-Fat High-Sucrose Dietary Model of Obesity in Wistar Rats”

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Background: Obesity is a multifactorial metabolic disorder characterized by excessive fat accumulation, dyslipidaemia, oxidative stress, chronic inflammation, and adipokine imbalance. A high-fat high-sucrose (HFHS) dietary model can mimic several metabolic alterations associated with obesity.

Objective: To formulate and characterize an HFHS diet and evaluate its ability to induce obesity-associated metabolic alterations in male Wistar rats.

Methods: The HFHS diet was formulated using standard rat feed (68%), vanaspati ghee (20%), sucrose (10%), cholesterol (1.5%), and sodium taurocholate (0.5%), with wheat flour as binder. Pellets showed hardness of 10.91 ± 0.28 kg/cm^2 and friability of 0.80 ± 0.05%. Twelve male Wistar rats were allocated to normal control (n=6) and HFHS (n=6) groups and fed for eight weeks. Anthropometric, biochemical, oxidative stress, adipokine, and histopathological parameters were evaluated. Data were expressed as mean ± SEM and analysed using one-way ANOVA followed by Tukey’s test.

Results: Compared with normal controls, HFHS-fed rats showed increased body-weight gain (202% vs 98%). Leptin increased from 20.65 to 165.12 pg/mL (~8-fold; $p<0.001$), whereas adiponectin decreased from 24.96 to 2.424 ng/mL (~90%; $p<0.001$). HFHS feeding also increased BMI, Lee index, adipose tissue weight, blood glucose, triglycerides, total cholesterol, LDL-C, hepatic and renal dysfunction markers, and lipid peroxidation, with reduced HDL-C, SOD, and CAT activities. Adipose tissue histopathology showed enlarged and irregularly arranged adipocytes with mild inflammatory infiltration.

Conclusion: The formulated HFHS diet produced an obesity-associated phenotype characterized by adiposity, metabolic dysregulation, oxidative stress, and adipokine imbalance in Wistar rats, supporting its use as a useful experimental model in this setting.



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Sciforum-211155: Effect of Myelopeptide 2 on Addiction Memory in the Mouse

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As is known, myelopeptides (MPs) influence the formation of long-term post-tetanic potentiation (LTP)—that is, they affect synaptic plasticity. To investigate the effect of MPs on the formation of addictive memory, we employed a morphine-induced conditioned place preference (CPP).

The experiment was conducted on male C57BL/6 inbred mice. Morphine hydrochloride (10 mg/kg, 100 µL) and MP2 (2 µg/kg, 50 µL) were dissolved in sterile 0.9% NaCl and administered intraperitoneally. CPP was established using a standard protocol for morphinization. Extracellular recording of excitatory postsynaptic potentials (EPSPs) was performed using glass microelectrodes placed in the stratum radiatum of the hippocampal slices CA1 region. Stimuls were applied to the Schaffer collateral region.

In control conditions, the amplitude of the field EPSP increased in 1.5 time after tetanization and remained elevated for 60 minutes or longer. Administration of MP2 during the conditioning phase blocked the acquisition of the conditioned place preference response and its subsequent recovery following extinction. MP2 completely blocks the formation of LTP in experiments on animal hippocampal slices during the conditioning stage corresponding to the acquisition of the morphine-induced conditioned place preference and the consolidation of addictive memory. The research was carried out within the state assignment of Ministry of Science and Higher Education of the Russian Federation for FRC FTM.

Author contributions: Writing - original draft, Gleb Volcho; Writing - review and editing, Nicolay Beregovoy;



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Sciforum-211252: An integrated *in silico* and bioactivity-based assessment of the potential thyroid-disrupting activity of UV filters

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The identification of potential endocrine-disrupting chemicals requires integrated approaches combining structural information, existing biological evidence, and targeted experimental testing. ToxTree, VEGA and thyroid-related ToxCast/ToxCast21 bioactivity data were used as complementary first-line *in silico* tools to evaluate ten selected UV filters: 2-ethylhexyl-4-methoxycinnamate (EHMC), 4-eminobenzoic acid (PABA), benzophenone, benzophenone-2 (BP-2), benzophenone-3 (BP-3), bezophenone-4 (BP-4), 4-methylbenzylidene camphor (4-MBC), avobenzone, homosalate and octocrylene. Propylthiouracil (PTU), resorcinol, and mefenamic acid were included as reference compounds with documented effects on thyroid-related processes, whereas 3,4-dichloroaniline was included as a presumed negative compound. ToxTree identified several not specific structural alerts in both the reference chemicals and the UV filters. VEGA did not identify reliable activity of any UV filter in the TRα or TRβ models while ToxCast/Tox21 data indicated potential TRα/TRβ antagonist activity for six UV filters, being octocrylene the most active. The strongest findings were obtained for BP-2, for which experimental data indicated DIO1 activity and a high-selectivity effect (HSE) on TPO, and for PABA, which was also experimentally classified as HSE for TPO. TTR-binding predictions were model-dependent: BP-3, avobenzone, and homosalate were predicted to be active with good reliability by the ONTOX model but inactive by the ED-Screen TTR model. Moreover, 3,4-DCA was classified as HSE for TPO with moderate reliability and associated with cytotoxicity according to ToxCast/Tox21, indicating that it should not be considered a universal negative control. Conversely, the ToxCast/Tox21 receptor signals were not corroborated by reliable VEGA TR predictions. Based on the combined bioactivity profiles, BP-2, BP-3, octocrylene and PABA emerged as the most priority UV filters for follow-up experimental testing.

Author contributions: Conceptualization, Montserrat Mitjans; Methodology, Elisabet Teixidó, Adriana Solange Maddaleno, Laia Guardia-Escote and Montserrat Mitjans; Software, Elisabet Teixidó; Validation, Elisabet Teixidó, Adriana Solange Maddaleno, Laia Guardia-Escote and Montserrat Mitjans; Formal analysis, Elisabet Teixidó, Adriana Solange Maddaleno, Laia Guardia-Escote and Montserrat Mitjans; Resources, Montserrat Mitjans; Data curation, Elisabet Teixidó, Laia Guardia-Escote and Montserrat Mitjans; Writing - original draft, Montserrat Mitjans; Writing - review and editing, Elisabet Teixidó, Adriana Solange Maddaleno, Laia Guardia-Escote and Montserrat Mitjans; Visualization, Elisabet Teixidó and Adriana Solange Maddaleno; Supervision, Montserrat Mitjans; Project administration, Elisabet Teixidó and Montserrat Mitjans; Funding acquisition, Elisabet Teixidó and Montserrat Mitjans;



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Sciforum-211311: Design of a Dual Adjuvant Multi-epitope Vaccine Candidate against *Helicobacter pylori*

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Despite the classification of *Helicobacter pylori* (*H. pylori*) as a Class I carcinogen affecting over half the global population, no licensed vaccine exists against this pathogen, and the rise in antimicrobial resistance continues to undermine standard eradication regimens. This study designed a novel dual adjuvant multi-epitope vaccine (MEV) candidate against *H. pylori*. The complete proteome of *H. pylori* strain 26695 was used to identify unique vaccine targets. Linear B-cell epitopes as well as HTL and CTL epitopes were predicted using BepiBLAST, NetMHCIIpan-4.3, and NetMHCpan-4.1, respectively. Predicted epitopes were further screened for antigenicity, allergenicity, and toxicity using VaxiJen, AllerTOP, and ToxinPred3.0. This pipeline identified four potential vaccine targets, where two most promising B-cell epitopes, one HTL epitope, and two CTL epitopes were selected and assembled into a recombinant MEV construct using linkers. Furthermore, Rv0652 and RS09 adjuvants were linked at the N and C termini of the vaccine, respectively, using appropriate linker sequences. Physicochemical analysis of the vaccine revealed a stable 204 amino acid construct of 20.69 κDa with an instability index of 23.57, a near-neutral GRAVY of 0.017, and an acidic theoretical isoelectric point of 5.06. Molecular docking of the MEV against the TLR-4/MD-2 complex yielded a highly favorable predicted binding, primarily mediated through hydrophobic interactions at the MD-2 binding interface. *In silico* immune simulation demonstrated that the vaccine elicited a robust humoral response, which was largely IgG1 dominated, and a strong B-cell memory following three doses. Results show that the MEV elicited a Th1-polarized response with sustained T-cell memory and a transient CD8+ response after the primary dose as well as a cytokine milieu dominated by IFN-γ and IL-2. These findings suggest that the designed MEV is a promising prophylactic vaccine candidate against *H. pylori* infection; as such, recombinant expression and subsequent preclinical studies are recommended.

Author contributions: Conceptualization, Mujahid Sani Nura; Methodology, Mujahid Sani Nura and Mansur Aliyu; Software, Mujahid Sani Nura; Validation, Mujahid Sani Nura and Mansur Aliyu; Formal analysis, Mujahid Sani Nura; Resources, Mujahid Sani Nura; Data curation, Mujahid Sani Nura; Writing - original draft, Mujahid Sani Nura; Writing - review and editing, Mujahid Sani Nura, Alhassan Sharif Abdullahi and Mansur Aliyu; Visualization, Mujahid Sani Nura; Supervision, Alhassan Sharif Abdullahi, Mansur Aliyu and Muhammad Adamu Abbas;



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Sciforum-211335: Epigenetic regulation as a new approach to gene therapy of uterine leiomyoma

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Introduction. Epigenetics of uterine leiomyoma (UL) cells has specific patterns causing dysregulation of proliferation and processing of steroid hormone receptors signals. Delivery of small interfering RNAs (siRNAs) against long non-coding RNAs (lncRNAs) can significantly improve the cell maintenance regulation and stop the tumor growth. In this work, originally designed peptide (cRGD-R6p) was used as a delivery system for siRNAs against regulatory molecules in UL cells.

Methods. Epigenetic targets (TET3, TET1, H19, SRA1, XIST, APTR) were selected based on literature data. Arginine-rich peptides modified with $\alpha\beta\nu3$ integrin ligand (cycloRGD) were synthesized and used as carrier system. The toxicity of siRNA/cRGD-R6p polyplexes to primary UL cells was tested. The effect of siRNAs delivery on UL cells proliferation was assessed by measuring metabolic activity (resazurin test). To assess the effect of steroid hormones (estrogen and progesterone) on cell proliferation during siRNA transfection, subsequent cell incubation was performed in the presence of hormones.

Results. Delivery of each selected siRNA resulted in a statistically significant decrease in UL cell proliferation. After incubating the cells with hormones, a significant reduction in proliferation was observed using siRNAs targeting SRA1 (estrogen) and XIST (estrogen and progesterone). By combining siRNAs against SRA1 and TET3, we achieved a synergistic effect in inhibiting proliferation.

Conclusion. Study shows that the use of siRNA targeting regulatory molecules suppresses UL cell proliferation both in the presence and absence of steroid hormones. Combining siRNAs can produce a synergistic effect, which offers a promising approach for UL therapy.

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Author contributions: Validation, Sofia Shtykalova; Investigation, Sofia Shtykalova; Data curation, Sofia Shtykalova; Writing - original draft, Sofia Shtykalova;



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Sciforum-211391: In vivo genotoxicity assessment of selected compounds for the development of HDAC4-targeting PROTACs in spinal muscular atrophy

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Progressive motor neuron loss and skeletal muscle atrophy are characteristic features of spinal muscular atrophy (SMA), a severe inherited neuromuscular disease. Despite significant advances in SMA treatment, there is still a need for the development and preclinical characterization of novel therapeutic strategies. Targeted protein degradation using proteolysis-targeting chimeras (PROTACs) represents a promising approach for modulating disease-relevant proteins. In particular, selective degradation of histone deacetylase 4 (HDAC4) has been proposed as a potential strategy for interfering with transcriptional pathways associated with muscle atrophy. Along with their pharmacological activity, the safety profile of newly developed PROTAC molecules represents an essential aspect of their preclinical evaluation. In the present study, the potential genotoxicity of two HDAC4-targeting PROTAC molecules, TG-49 and PJ-653, was investigated *in vivo* using Wistar rats. DNA damage was evaluated by the alkaline comet assay, which enables sensitive detection of DNA strand breaks and related lesions at the level of individual cells. Animals treated with ethyl methanesulfonate (EMS), a well-established genotoxic agent, were included as a positive control, while an appropriate untreated control group was used for comparison. Neither TG-49 nor PJ-653 induced significant DNA damage in the liver, kidney, or femur samples compared with the control groups, indicating that the investigated compounds did not exhibit detectable genotoxic effects in the evaluated tissues under the applied *in vivo* conditions. The obtained results contribute to the safety characterization of TG-49 and PJ-653 and provide additional information relevant to their further preclinical development as potential HDAC4-targeting agents for SMA.

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Author contributions: Conceptualization, Milan Mladenović; Methodology, Nevena Tomašević, Gordana Tasić, Predrag Jovanović, Milena R Simić, Vladimir Savić, Sanja Lj Matić and Milan Mladenović; Software, Milan Mladenović; Investigation, Sanja Lj Matić; Resources, Gordana Tasić, Predrag Jovanović, Milena R Simić and Vladimir Savić; Data curation, Sanja Lj Matić; Writing - original draft, Nevena Tomašević, Sanja Lj Matić and Milan Mladenović; Writing - review and editing, Nevena Tomašević, Sanja Lj Matić and Milan Mladenović; Visualization, Sanja Lj Matić; Supervision, Milan Mladenović; Project administration, Milan Mladenović;



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Sciforum-211540: Electrochemical evaluation of the antioxidant capacity of medicinal plant micellar extracts

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Medicinal plants are one of the sources of bioactive components, which extraction can provide novel substances for the drug development. The use of sonication-assisted extraction of antioxidants from medicinal plants using surfactant micellar media is developed for the first time. The surfactant nature (cationic, non-ionic, and anionic) effect was tested, and the data obtained were compared to traditional ethanolic extracts. Non-ionic surfactants are the most effective. According to coulometric titration with electrogenerated titrants (bromine and hexacyanoferrate(III) ions), Triton X-100 (10 mM) is the best extractant providing 1.7–6.5-fold higher yield of antioxidants *vs*. ethanol. The obtained total antioxidant capacity and ferric reducing power of the extracts indicate total content of the antioxidants of various classes and the total content of phenolic antioxidants in the sample, respectively. A two-step chronoamperometric method at the electrode modified with MnO_2 nanorods was developed for antioxidant capacity evaluation of the medicinal plant micellar extracts. The electrode was characterized by scanning electron microscopy, electrochemical impedance spectroscopy, and voltammetry. A two-step chronoamperometry at 0.35 and 0.75 V for 50 s each allows assessment of the contribution from the antioxidants of different powers to the antioxidant capacity of the samples. Electrochemical approaches were used for screening of 24 samples of commercial medicinal plants of various species used in phytotherapy. The plant parts included bark, shoots, rhizomes and roots, leaves, herb, flowers, fruits, etc. The highest antioxidant parameters were obtained for *Bergenia crassifolia* (L.) Fritsch rhizomes, *Vaccinium vitis-idaea* L. leaves, *Ledum palustre* L. shoots, and *Sanguisorba officinalis* L. rhizomes and roots that agrees well with their phytochemical profile.

Author contributions: Conceptualization, Guzel Ziyatdinova; Methodology, Guzel Ziyatdinova; Validation, Guzel Ziyatdinova and Elizaveta Krasilni'kova; Investigation, Elizaveta Krasilni'kova; Writing - original draft, Guzel Ziyatdinova; Writing - review and editing, Guzel Ziyatdinova; Visualization, Guzel Ziyatdinova and Elizaveta Krasilni'kova; Supervision, Guzel Ziyatdinova;



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Sciforum-211620: Impact of Poirier-Bienvenu Neurodevelopmental Disease-associated Variants on CK2 Holoenzyme Assembly

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Protein kinase CK2 is a constitutively active and highly conserved serine/threonine kinase that is ubiquitously expressed in eukaryotic cells.[1] It functions as a heterotetrameric holoenzyme composed of two catalytic subunits (α or α′) and two regulatory β subunits.[2] Mutations in *CSNK2B*, the gene encoding CK2β, cause Poirier-Bienvenu neurodevelopmental syndrome (POBINDS), a disorder characterized by early-onset epilepsy, variable intellectual disability, language impairment, and, in some cases, physical disabilities and psychiatric manifestations.[3] [4]

To investigate whether POBINDS-associated mutations affect holoenzyme assembly 12 variants located within regions implicated in α/β or β/β interaction, including the αF helix, hairpin loop and zinc finger domain, were selected for functional characterization. All variants located within regions important for holoenzyme formation exhibited reduced affinity for the α subunit. In addition, kinase activity was reduced for most variants. The α/β interaction was subsequently investigated by determination of dissociation constants (K_D). Dimerization and holoenzyme assembly were assessed by size-exclusion chromatography. Surprisingly, the C137G variant retained the ability to form intact holoenzymes and dimers, which was further confirmed by negative-stain electron microscopy. These findings indicate that POBINDS-associated mutations in structurally important regions of CK2β can impair α/β subunit interaction and CK2 function, while the preserved assembly observed for C137G suggests that individual variants may affect CK2 through distinct molecular mechanisms.

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Author contributions: Conceptualization, Johanna Marie Fellhölter; Methodology, Johanna Marie Fellhölter, Sandra Jordan, Christian Werner and Alexander Gast; Formal analysis, Johanna Marie Fellhölter, Christian Werner and Alexander Gast; Investigation, Johanna Marie Fellhölter, Sandra Jordan and Christian Werner; Writing - original draft, Johanna Marie Fellhölter and Christian Werner;



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Session 3. New Small Molecules as Drug Candidates

Sciforum-201826: Oligopeptide based ternary chelators of transition metal ions as complexes for managing aggregation and redox processes of Alzheimer's disease pathogenesis

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The study deals with theoretical and experimental structural analysis via mass spectrometry and nuclear magnetic resonance of complexes of competitively interacting oligopeptides with Cu(I/II) and Zn(II) ions; thus, producing innovative species as prospective candidate therapeutics governing aggregation and catalyzed reactive oxygen reactions of the Alzheimer's disease. There is peptide coordination with Cu(I/II) ions; thus, preventing Cu(II)-amyloidal-beta (Ab) complex formation as a prospective therapeutic approach. It improves therapeutics-like property of oligopeptides and tackles metal ion selectivity. Further, ologopeptides appear selective toward Cu(II)-ion in presence of Zn(II)-one. The theme is crucial for efficacious management of neuromodulated processes, because not only Alzheimer's disease, but also neurodegenerative disorders exhibit similar protein aggregation reactions. An in-depth understanding of interactions of oligopeptides, Cu(I/II), and Zn(II)-ions; thus, preventing Cu(II)-Ab formation improves medication administration. Scarce data on Cu(II)-oligopeptide therapeutics occur. Proteins are key macromolecules in Alzheimer's disease pathology. This research achieves integrated knowledge of metalloproteins involved in Alzheimer's disease and based on Cu(II)-peptide complexes. It challenges both the fundamental and applied science. In vivo processes via mimic of biomacromolecular structures entail synthetic oligopeptides joined with transition metal ions. Ternary metal-peptide complexes mimic active sites. Further, Cu(I/II)-Aβ interaction with molecular oxygen is implicated into fibrillization of Aβ-peptides as a hallmark of Alzheimer's disease pathology. Data on Cu(I/II)-Aβ-peptide-O2 intermediates crucially fill the gap of knowledge of hCu(I/II) ions modulated Aβ-peptides reactions. In addition to aforementioned robust methods for structural analysis of chemicals, there are also utilized high accuracy approaches to quantum chemistry.



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Sciforum-202453: Turning Down ROCK Signaling in Pulmonary Fibrosis: Novel 1,2,4-Triazole-Based Antifibrotic Candidates

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Can a subtle chemical modification retune a kinase inhibitor toward a different kinase target? This question guided our investigation into the development of novel Rho-associated coiled-coil-containing protein kinase (ROCK) inhibitors as potential antifibrotic agents.

Pulmonary fibrosis is a chronic and life-threatening disorder affecting up to 0.1% of the global population and associated with poor prognosis and limited survival. This disease is characterized by excessive extracellular matrix deposition, progressive tissue remodeling, and irreversible loss of lung function [1]. Although current antifibrotic therapies, including nintedanib and pirfenidone, can slow disease progression, they are unable to reverse established fibrosis, highlighting the need for new therapeutic strategies [1].In this context, ROCK1 and ROCK2 have emerged as key mediators of profibrotic signaling and fibroblast activation, making these kinases attractive pharmacological targets [2].

Thus, we started from 1,2,4-triazole-based kinase inhibitors previously developed by our group [3] and modified their structure to redirect their activity toward ROCK inhibition. Specifically, isosteric replacement, combined with modulation of the terminal region, led to a new series of 1,2,4-triazole derivatives [4].

Enzymatic profiling, *in silico* studies, and functional evaluation in a cellular model of fibrosis identified promising compounds, with selected derivatives showing greater antifibrotic activity than nintedanib under the same experimental conditions.

Overall, these preliminary results warrant further investigation to characterize the activity of this series and assess its broader potential for antifibrotic applications.

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Sciforum-207760: In Silico Screening of the MolPort Natural Product Database to Identify Potential Lyn Tyrosine Kinase Inhibitors for the Treatment of Triple-Negative Breast Cancer

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Triple-Negative Breast Cancer (TNBC) poses a significant global health challenge due to its aggressive clinical behavior, high recurrence rates, and the limited effectiveness of available therapeutic options. This study aims to identify bioactive Natural compounds with potential inhibitory effects against Lyn tyrosine kinase, a key enzyme implicated in the pathogenesis of TNBC. Online servers including Molport, Permit, SWISSADME, and ProTox-iii were employed to screen the compounds. Ten thousand natural bioactive compounds were successfully retrieved from the Molport Natural Compound Database. Compounds were screened for structural similarity to the co-crystallized ligand (Dasatinib), toxicity, and ADME properties, after which 68 compounds were selected for further studies. Docking was performed using AutoDock Vina, and Molecular Dynamics simulations were performed using GROMACS 2026.2. Docking studies showed binding energy values ranging from -6.9 to -9.7 kcal/mol, comparable to the co-crystallized ligand, which had a binding affinity of -9.7 kcal/mol. The most notable interactions are ASP329, LEU275, LYS253, GLU290, MET322, and THR319, which interact via pi-cation and van der Waals interactions. Lig28 interacted with key amino acid residues, including LEU253, MET322, LYS275, and THR319, via pi-alkyl, pi-cation, and van der Waals interactions. ADMET profiling and docking results further prioritized the Lig28 molecule. Molecular dynamics simulations confirmed its potent predicted inhibitory activity and complex stability against the target. These findings highlight the potential of these identified compounds as promising Lyn Kinase inhibitors for TNBC therapy, offering a strategic avenue to combat resistance mechanisms. Further experimental validation is warranted to translate these computational insights into therapeutic candidates.

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Sciforum-207843: Natural Product-Based Antileishmanial Drug Discovery – Preliminary *in silico* study

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Leishmaniasis is a neglected tropical disease caused by *Leishmania* parasites and transmitted through the bite of infected sand flies. Depending on their clinical manifestations, leishmaniases are classified into three major forms: cutaneous, mucocutaneous, and visceral, the latter being fatal if left untreated. In addition to its impact on human health, leishmaniasis is also a significant veterinary concern, particularly in dogs infected with *L. infantum*, which serve as the main reservoir hosts. In the context of global warming, the geographical expansion of sand fly vectors has increased the risk of disease spread, further emphasizing the importance of effective control strategies. Despite this growing threat, safe, effective, and affordable treatments for parasitic infections remain limited. Currently available antileishmanial drugs are associated with major drawbacks, including toxicity, high cost, prolonged treatment regimens, and the emergence of drug resistance. These limitations have driven extensive efforts toward the discovery and development of novel antileishmanial agents with improved safety and efficacy profiles. Among the promising candidates, steroid-based compounds have attracted considerable attention from pharmacologists, chemists, and biochemists because of their broad therapeutic potential. In addition to their diverse biological activities, steroid derivatives have demonstrated significant antiparasitic properties, including promising antileishmanial activity.

The steroid compounds investigated by our research group are initially designed as potential anticancer agents. Taking into account their biological potential, a rational approach was to employ different disciplines to identify promising steroid-based compounds as safe and efficient antiparasitic agents. In the present study, a series of ten derivatives bearing different carbamate groups was subjected to *in silico* predictions of antileishmanial activity, relevant human protein targets, and toxicity profiling, using available online tools such as Way2Drug-Pass online, ADMETlab 2.0 and SwissADME. Only one compound showed the best properties both in terms of potential antileishmanial activity and in terms of safety and oral bioavailability.

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Sciforum-208315: Mutagenicity assessment of novel nitroimidazooxazole anti-infective candidates using the Ames Test

Manoela de Araújo Gonçalves [1], Isabelle Guerreiro Moreira [1], Nicole Pichirilli Catirce [1], João Lucas Bruno Leandro dos Santos [2], Cauê Benito Scarim [3], Jean Leandro Dos Santos [3]* and Flavia Aparecida Resende [1,]*

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Nitroimidazole-based compounds are widely explored as anti-infective agents, although their nitro group may be associated with genotoxicity concerns. Here, we investigated the mutagenic profile of ten nitroimidazooxazole derivatives (49–58) previously developed for antimycobacterial and antileishmanial applications. The compounds were evaluated by the Ames test using Salmonella Typhimurium strains TA98, TA97a, TA100, and TA102, with and without metabolic activation by S9. Five concentrations were tested, from 31.25 to 250 μg/plate, using the pre-incubation protocol, with assays performed in triplicate. Mutagenicity was evaluated using revertant colony counts, dose-response trends, statistical comparisons with the negative control, and the mutagenicity index. Across all strains and experimental conditions, none of the compounds produced a significant increase in the number of revertants. The mutagenicity index remained below 2 at every concentration tested, and no consistent concentration-dependent response was observed. The expected responses obtained with the positive controls confirmed the validity of the assays. Taken together, these results show that derivatives 49–58 did not exhibit mutagenic activity in the bacterial reverse mutation assay, regardless of metabolic activation, supporting their continued preclinical evaluation as anti-infective candidates.

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Sciforum-208406: Evaluation of the antinociceptive and anti-inflammatory activity of 2-morpholinoethyl 2-(naphthalen-2-yloxy)acetate and 2-(piperidin-1-yl)ethyl 2-(naphthalen-2-yloxy)acetate as novel Sigma-1 receptor antagonists

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The sigma-1 receptor represents a highly promising therapeutic alternative to classical opioids and NSAIDs for the management of pain and inflammation. The development of highly selective compounds with optimal pharmacokinetic profiles remains a critical challenge in medicinal chemistry. In this study, novel ligands were designed through a pharmacophoric hybridization strategy based on the Glennon model, coupling the naphthalene nucleus of S1RA with haloperidol-derived cyclic amines via an ester linker. Following computational validation through molecular docking at the sigma-1 receptor, two main molecules were chemically synthesized: Piperiéster (piperidine derivative) and Morfoéster (morpholine derivative). Their biological efficacy was subsequently evaluated **in vivo** using murine models of pain (hot plate and formalin tests) and inflammation (croton oil-induced auricular edema and carrageenan-induced plantar edema). It was observed that both molecules showed a clear dose-dependent antinociceptive effect in the hot plate test, reaching 80-90% efficacy, indicating their ability to cross the blood-brain barrier. In the formalin model, Morfoéster proved superior for inflammatory pain, achieving nearly 70% inhibition in Phase II, characteristic of central sensitization blockade. Conversely, in systemic inflammation evaluations (plantar edema), Piperiéster exhibited a remarkable 81% inhibition. Both compounds also successfully reduced topical inflammation by more than 70% in the auricular edema model. These results allow us to conclude that the hybridization strategy successfully yielded novel sigma-1 receptor ligands with proven biological activity. Morfoéster emerges as an optimal clinical tool for central and inflammatory pain, while Piperiéster demonstrates a notable capacity to curb systemic inflammation. Both derivatives represent excellent starting points for the development of safer new therapies without the side effects of conventional treatments.

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Sciforum-209217: E2F-Driven Proliferative Transcription Characterizes an MK-2206-Sensitive AML State and Is Suppressed Following AKT Inhibition

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Background: Acute myeloid leukemia (AML) is a heterogeneous hematologic malignancy in which dysregulated survival, proliferation, and metabolic signaling contribute to treatment resistance. The PI3K/AKT/mTOR pathway is frequently implicated in leukemic cell survival, making AKT inhibition a potential therapeutic strategy. This study aimed to identify transcriptomic features associated with sensitivity to MK-2206, a selective allosteric AKT inhibitor, in AML.

Methods: Publicly available pharmacogenomic and transcriptomic datasets were integrated to characterize molecular features associated with MK-2206 response. Baseline gene-expression profiles from six AML cell lines were analyzed with MK-2206 IC50 values and classified as sensitive or resistant using a three-versus-three comparison. Differential expression analysis was performed between sensitive and resistant cell lines, while GSE172189 was used to assess transcriptional changes following MK-2206 exposure. Baseline and treatment-associated differentially expressed genes were integrated to identify overlapping MK-2206-associated genes. A stricter fold-change threshold defined a 15-gene sensitivity-associated subset. Functional enrichment, gene set enrichment analysis, and network analysis were subsequently performed.

Results: Integration identified 162 overlapping MK-2206-associated genes, from which a stricter threshold defined a 15-gene subset that distinguished sensitive from resistant AML cell lines. Network analysis revealed functional associations with energy metabolism, DNA replication, cell-cycle regulation, chromosomal organization, and vesicular trafficking, with **YWHAE** emerging as a highly connected node. Functional annotation of the broader gene set implicated Rho GTPase signaling, apoptosis, interferon response, DNA repair, and cell-cycle checkpoint regulation. Gene set enrichment analysis demonstrated suppression of MYC/E2F-associated proliferation, DNA replication, DNA repair, G2/M checkpoint, mitotic spindle, and oxidative phosphorylation programs following MK-2206 exposure, alongside activation of stress-response pathways including unfolded protein response and p53-associated DNA-damage signaling.

Conclusion: MK-2206 sensitivity in AML appears to reflect a broader transcriptional state involving proliferative, metabolic, genome-maintenance, apoptotic, interferon-related, and cellular stress-response programs rather than dependence on a single gene.

Author contributions: Methodology, ayriana safari baesmat; Software, ayriana safari baesmat; Formal analysis, ayriana safari baesmat; Investigation, ayriana safari baesmat; Writing - original draft, ayriana safari baesmat; Visualization, ayriana safari baesmat;



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Sciforum-209844: Targeting Transcription in Neuroblastoma: Development of Inhibitors of Non-POU Domain-Containing Octamer-Binding Protein NONO

Sophia S. Borisevich [1, 2], Denis A. Tiunov [3], Sofya S. Pogodaeva [4], Lidia V. Mammadova [5], Alexander A. Kurkin [3], Oleg A. Kuchur [5], Alexander A. Shtil [6, 7]*

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The non-POU domain-containing octamer-binding protein (NONO emerges as a master regulator of gene expression in physiological states and an anticancer target. Phenotypic screening identified (R)-4-(2-chloroacetyl)-N-(4-methoxybenzyl)-1-((4-methoxyphenyl)sulfonyl)piperazine-2-carboxamide ((R)-SKBG-1)) as a pioneer pharmacological NONO inhibitor. Herein we, for the first time, report a thrifty synthetic route to (R)-SKBG-1 from the available (R)-(*tert*-butoxycarbonyl)piperazine-2-carboxylic acid. In search of structure-activity relationship within the (R)-SKBG-1 chemotype, we synthesized a series of original derivatives. For docking into the model of the NONO homodimer, the geometrical parameters of the complex (R)-SKBG-1–NONO were minimized using OPLS4 force field. Covalent docking was performed using Glide algorithm. Docking poses were ranged according to IFD score. These procedures revealed that the covalent bond between the chloroacetyl moiety at the position 4 of the piperazine ring ('warhead') and Cys145 residue proved to be mandatory for NONO inhibition. The cytotoxicity was assessed by MTT tests, colony formation assays and flow cytometry assisted analysis of cell death (YO-PRO-1/propidium iodide staining). NONO inhibition was translated into preferential potency for human neuroblastoma cell lines Kelly, SH-SY5Y, SK-N-AS and SK-N-SH (at low micromolar concentrations) compared to non-malignant, bone marrow derived HS-5 fibroblasts. Molecular dynamics simulations of NONO-RNA complexes were analyzed based on RMSD and RMSF fluctuations and time of contact between ligand atoms and neighboring amino acid residues; ΔG_{bind} values for representative clusters were estimated by MM-GBSA method (solvent: water). We found that binding to Cys145 ensured the close proximity of (R)-SKBG-1 to critical Phe residues involved in protein-RNA interaction. The derivative with the acryloyl moiety at the position 4 of the piperazine ring formed the covalent bond with Cys145 via Michael addition and was indiscriminately potent for tumor and non-malignant cell lines. In contrast, modifications of the chloroacetyl fragment with propionyl, trifluoroacetyl or cyclopropionyl moieties led to a significant decrease of cytotoxicity since these compounds were unable to bind Cys145. Thus, binding to Cys145 and stable ligand positioning in the binding cavity are necessary and sufficient for NONO inhibition and neuroblastoma cell death.

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Sciforum-209922: Novel Sila-Vitamin D Derivatives Targeting the Vitamin D Receptor for Application in Cancer Therapy

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Cancer is a highly complex disease that affects millions of people worldwide, with nearly 20 million new cases reported in 2022. Despite significant advances, current treatments remain insufficient. In this context, the vitamin D receptor (VDR), a nuclear receptor involved in several biological processes, has emerged as a promising target for cancer therapy. Although calcitriol ($1,25D_3$) and other VDR agonists have shown therapeutic potential, their clinical application is limited by severe hypercalcaemic effects.

Here, the strategic incorporation of silicon into $1,25D_3$ was explored for the first time. To this end, six novel analogues of $1,25D_3$, in which a silicon atom was introduced as an isosteric replacement at the C25 position of the side chain, were rationally designed, synthesised, and biologically evaluated.

The designed sila-derivatives were successfully synthesised via a Wittig-Horner approach from the Inhoffen-Lythgoe diol. Structural studies of VDR complexes with the sila-derivatives revealed favourable interactions between the modified side chains and the VDR ligand-binding domain. Functional assays demonstrated that the analogues retained VDR-mediated activity while exhibiting markedly lower hypercalcaemic effects than $1,25D_3$. Their biological effects were further investigated in cancer cell lines (HaCaT, SKOV-3, PC-3, MCF-7, and MDA-MB-231 cells), where, in combination with conventional chemotherapeutics, the analogues significantly reduced cancer cell proliferation, suggesting potential synergistic effects.

Overall, these results highlight the potential of silicon-modified secosteroidal VDR ligands and support further investigation of sila-vitamin D derivatives for applications in cancer-related contexts.

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Sciforum-209961: Comparative Assessment of Cognitive Effects of Anthranilamide Derivatives

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Anthranilamides have attracted increasing attention due to their antispasmodic and anti-inflammatory effects. Preclinical evidence suggests that these compounds may affect acetylcholinesterase activity, which could indirectly enhance cognitive performance. Therefore, the present study aimed to comparatively evaluate the effects of three previously synthesized anthranilamides, namely 2-chloro-N-(2-(phenethylcarbamoyl)phenyl)benzamide (**1**), 2-amino-N-(3-chlorophenethyl)benzamide (**2**), and 2-(2-chloro-2-phenylacetamido)-N-(3,4-dimethoxyphenethyl)benzamide (**3**), on cognitive functions in rats and to find them as potential active substances for neurodegenerative diseases treatment. In silico calculations, using SwissADME, Pro-Tox II, and PASS online, were performed. Two-way active avoidance test, activity cage test, and two passive avoidance tests – step-through and step-down test, were conducted. Overall, the obtained results imply that the anthranilamide scaffold has effects on cognitive processes, but these effects can be significantly altered by structural modifications. Our results demonstrate that anthranilamide derivatives do not produce a pronounced depressant or stimulant effect on the central nervous system. Two of the compounds, (**1**) and (**2**), showed cognitive-enhancing properties, with effects varying depending on the behavioral test applied, while compound (**3**)'s structural features might be less promising for this activity. These findings highlight the potential of specific anthranilamide derivatives as modulators of learning and memory processes. Therefore, the current results offer an initial SAR framework for more anthranilamide derivative improvement.

Author contributions: Conceptualization, Miglena Milusheva, Darinka Slavcheva Dimitrova and Stoyanka Atanasova Nikolova; Methodology, Miglena Milusheva, Darinka Slavcheva Dimitrova, Kremena Saracheva, Vera Nikolaeva Gledacheva and Iliyana Dimitrova Stefanova; Validation, Darinka Slavcheva Dimitrova, Vera Nikolaeva Gledacheva and Iliyana Dimitrova Stefanova; Formal analysis, Miglena Milusheva, Darinka Slavcheva Dimitrova, Kremena Saracheva and Vera Nikolaeva Gledacheva; Investigation, Darinka Slavcheva Dimitrova, Kremena Saracheva, Vera Nikolaeva Gledacheva and Iliyana Dimitrova Stefanova; Data curation, Darinka Slavcheva Dimitrova and Kremena Saracheva; Writing - original draft, Miglena Milusheva, Darinka Slavcheva Dimitrova, Kremena Saracheva and Iliyana Dimitrova Stefanova; Writing - review and editing, Miglena Milusheva, Darinka Slavcheva Dimitrova, Vera Nikolaeva Gledacheva and Stoyanka Atanasova Nikolova; Visualization, Miglena Milusheva, Darinka Slavcheva Dimitrova, Kremena Saracheva and Vera Nikolaeva Gledacheva; Supervision, Stoyanka Atanasova Nikolova; Project administration, Darinka Slavcheva Dimitrova and Stoyanka Atanasova Nikolova;



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Sciforum-210019: Peptide Engineering Strategies for AT1R: Structure-Based Analysis of Angiotensin II Analogues

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The angiotensin II type 1 receptor (AT1R) is a Class A G protein-coupled receptor activated by the endogenous octapeptide angiotensin II (Ang II) and plays a central role in blood-pressure regulation, fluid homeostasis and cardiovascular signalling. The well-characterised peptide–receptor system provides a useful model for investigating how defined peptide modifications influence GPCR recognition.

In this study, Ang II was used as a reference scaffold for the structure-based design of peptide analogues with altered conformational and physicochemical properties. The investigated strategies included head-to-tail cyclisation, introduction of D-amino-acid residues and N-terminal truncation. Molecular docking with AT1R was used to compare the resulting binding poses, receptor-contact patterns and the preservation or redistribution of key peptide–receptor interactions.

The head-to-tail cyclic analogue showed the most favourable docking performance compared with native Ang II. It retained favourable AT1R interactions while displaying a modified hydrogen-bond and hydrophobic contact pattern, suggesting that cyclisation can influence peptide–receptor recognition

The comparative analysis is intended to identify which peptide-engineering strategies preserve favourable AT1R recognition while modifying peptide conformation. These results may provide a basis for further molecular dynamics studies and for the rational design of conformationally controlled peptide ligands targeting AT1R.

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Sciforum-210096: Design of Potential Antimalarial Molecules Using QSAR, Molecular Docking and Molecular Dynamics Techniques

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Malaria is a serious and potentially fatal tropical disease caused by parasites of the genus Plasmodium, transmitted to humans by the bite of infected Anopheles mosquitoes. There has recently been a growing emergence of strains resistant to current treatments, and synthetic analogues of bestatin, its natural inhibitor, have been designed using the four-component Ugi reaction (Ugi-4C), which has great combinatorial capabilities, to combat them. The objective is to design new inhibitors for malaria treatment using the capabilities of the Ugi-4C reaction. For library construction, the RDKit library was used. The complete set was evaluated by molecular docking (with AutoDock Vina, using the AD4 scoring function) and quantitative structure–activity relationship (QSAR) models. The library was studied with MAIP QSAR. Molecular dynamics simulations of some ligands of 1 ns duration were performed using NAMD software. A library of 245 compounds was built. Taking into account the energies obtained from molecular docking and the QSAR score, 8 inhibitor candidates were selected. From the molecular dynamics simulations performed on the 8 candidates, a root-mean-square deviation (RMSD) between 1–3 Å and a root-mean-square fluctuation (RMSF) in the ranges of 1–3 Å were obtained. The selected inhibitors adopt conformations stabilized by interactions with key residues of the active site (His-496, Asp-581, and Gly-460) and by coordination with the zinc ion present in the enzyme target. The RMSD and RMSF values evidenced the formation of stable complexes and limited conformational fluctuation.



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Sciforum-210134: A multi-action Pt(IV) prodrug against aggressive cancer cells

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Glioblastoma and malignant mesothelioma are highly aggressive tumors characterized by therapeutic resistance and poor prognosis. To address these challenges, the Pt(IV) prodrug, Pt(IV)Ac-POA, where cisplatin is linked to the histone deacetylase inhibitor (HDACi) 2-(2-propynyl)octanoic acid (POA), was investigated. The compound takes advantage of its lipophilicity which enhances cell uptake, while the HDACi promotes chromatin decondensation, increasing DNA sensitivity to platination. Following preliminary studies on multiple cell models, the effects on human glioblastoma and human biphasic mesothelioma were investigated. Results demonstrated that Pt(IV)Ac-POA triggers various regulated cell death pathways, such as apoptosis, autophagy, necroptosis, and ferroptosis, often outperforming standard cisplatin. Moreover, the compound suppressed DNA repair mechanisms. Studies on glioblastoma cells also revealed the advantages of combining chemotherapy with mycotherapy and, above all, with hadrontherapy (carbon ion radiotherapy). This integrated protocol further reduced clonogenicity and amplified long-term antitumor effects compared to single-agent treatments, thus representing a promising strategy to improve therapeutic outcomes.



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Sciforum-210299: QSAR Analysis of Substituted Cinnamic Acid Derivatives with Antibacterial Activity

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Background: Antimicrobial resistance continues to demand efficient discovery strategies. Phenylpropanoid scaffolds, such as cinnamic acid derivatives, exhibit a broad spectrum of antimicrobial potential.

Aim: to construct and validate a QSAR model for substituted cinnamic acid derivatives and to identify molecular descriptors associated with their antibacterial activity.

Methods: Chemical structures and antibacterial activities for 32 literature-derived cinnamic-acid derivatives were compiled; activity was expressed as log(1/MIC). The dataset comprised 22 learning and 10 test compounds. Three-dimensional structures were optimized in HyperChem using MM+ molecular mechanics followed by semi-empirical optimization. A total of 4,885 molecular descriptors were calculated using Dragon 7. Prior to modeling, descriptor data were standardized and low-variance variables were removed. Non-linear QSAR models were constructed in Statistica 13 using Multivariate Adaptive Regression Splines (MARSplines), which represent predictor effects by piecewise basis functions separated by data-dependent knots. Model construction involved generation of basis functions followed by pruning of less informative terms. Models with different interaction orders and numbers of basis functions were compared using R^2, leave-one-out Q^2, and mean absolute error (MAE); residual normality was assessed using the Shapiro–Wilk test.

Results: The selected additive MARSplines model (interaction order 1; 12 basis functions) yielded R^2 = 0.9720, Q^2(LOO) = 0.9995, and MAE = 0.0662. The model included 12 descriptors representing complementary structural properties: Geary autocorrelations GATS2e and GATS5e weighted by Sanderson electronegativity; GATS6s and GATS8s weighted by intrinsic state; Moran autocorrelation MATS3i weighted by ionization potential; 3D-MoRSE descriptors Mor26s and Mor32u; radial distribution functions RDF110m, RDF130e, and RDF130v weighted by atomic mass, electronegativity, and van der Waals volume, respectively; the valence-state descriptor SssCH; and Eig14_AEA. The MARS equation revealed descriptor-specific threshold effects, with predictor contributions changing after the corresponding knot values were exceeded.

Conclusions: The MARSplines QSAR model identified non-linear associations between antibacterial activity and molecular features describing topological autocorrelation, intrinsic state, ionization potential, three-dimensional molecular information, and radial distributions of atomic properties. These results provide an interpretable description of structural features associated with antibacterial activity within the investigated series of cinnamic-acid derivatives.



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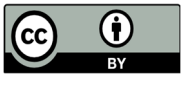
Sciforum-210306: Modulating effect of low-molecular allosteric regulators of the thyroid-stimulating hormonereceptor on thyroid function in rats exposed to low temperatures

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Antithyroid drugs are widely used for the pharmacological correction of hyperthyroidism; however, they have numerous side effects and do not act on the key component of the thyroid axis—thyroid-stimulating hormone receptors (TSHR). Allosteric antagonists and negative modulators of TSHR can be used to reduce TSHR activity, including the thieno[2,3-d]thienopyrimidine derivatives TPY1 and TPY4, which we developed previously [1]. The most suitable model of physiologically induced hyperthyroidism is cold-induced triiodothyronine (T3) hyperthyroidism. The aim of this study was to evaluate the pharmacological properties of TPY1 and TPY4 as negative modulators of TSHR in a rat model of cold-induced T3 hyperthyroidism. After 10 days of low-temperature exposure (+5 °C), T3 hyperthyroidism with increased total T3 (tT3) levels and the tT3/tT4 ratio was observed, while after 15 days, the tT3 level did not differ from the control, but the tT3/tT4 ratio remained high due to T4 deficiency. A single treatment with TPY1, an allosteric antagonist of TSHR (15 mg/kg, intraperitoneally), prevented T3 hyperthyroidism after 10 days, but caused a pronounced thyroxine deficiency and suppression of thyroid function after 15 days of cold exposure. TPY4 (15 mg/kg, intraperitoneally) attenuated, albeit to a lesser extent, T3 hyperthyroidism after 10 days, but after 15 days of cold exposure it did not worsen, but restored, thyroxine deficiency, exhibiting the properties of a negative allosteric modulator and TSHR agonist (ago-NAM). This effect was maintained after five days of TPY4 administration. Thus, TPY4, the N-tert-butylamide of 5-amino-4-(4-bromophenyl)-2-(methylthio)thieno[2,3-d]pyrimidine-6-carboxylic acid, can be used to correct moderate hyperthyroidism without causing thyroid hormone deficiency. The work was supported by the state assignment of the Institute of Evolutionary Physiology and Biochemistry of the Russian Academy of Sciences (No. 075-00264-26-00). [1]. Derkach K.V., Didenko E.A., Sorokoumov V.N., Zakharova I.O., Shpakov A.O. Low-molecular-weight ligand of the thyroid-stimulating hormone receptor with the activity of a partial agonist and a negative allosteric modulator // Doklady Biological Sciences. - 2025. - Vol. 520. - N. 1. - P. 122-127. doi: 10.31857/S2686738925010208

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Sciforum-210376: Molecular Docking Studies of Natural Compounds Targeting Diabesity in Polycystic Ovary Syndrome via the AMPK Pathway

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Polycystic Ovary Syndrome (PCOS) is a common endocrine and metabolic disorder characterized by insulin resistance, obesity, and hormonal imbalance, which collectively contribute to the development of diabesity. AMP-activated protein kinase (AMPK) plays a crucial role in regulating glucose and lipid metabolism and has emerged as a promising therapeutic target for the management of metabolic disturbances associated with PCOS. This study aimed to investigate the potential of selected natural compounds as modulators of AMPK-related protein targets using molecular docking approaches.A total of seventy-five natural compounds with reported antidiabetic, anti-obesity, and insulin-sensitizing activities were selected from literature and public databases. The compounds were prepared and optimized using Molecular Operating Environment (MOE) software and docked against two experimentally determined human AMPK structures, PDB IDs 4CFE and 5ISO. Physicochemical properties, drug-likeness, absorption, distribution, metabolism, excretion (ADME), and toxicity profiles of selected lead compounds were further evaluated using SwissADME and ProTox-II. The docking results with 4CFE and 5ISO revealed that the natural compounds Rutin, Curcumin and Silibinin demonstrated notable binding affinities, and they emerged as the top-performing compounds in the study. Physicochemical and ADME analyses indicated that Curcumin and Silibinin possessed favorable drug-likeness characteristics, acceptable bioavailability, and promising pharmacokinetic profiles. Toxicity prediction revealed acceptable safety profiles for the selected lead compounds, with no predicted carcinogenic or mutagenic effects. The findings suggest that Curcumin and Silibinin emerged as the most promising lead compounds for the management of diabesity associated with PCOS due to their favorable binding affinities, physicochemical properties, pharmacokinetic characteristics, and predicted safety profiles.

Keywords: Polycystic Ovary Syndrome, PCOS, Diabesity, AMPK, Molecular Docking, Curcumin, Silibinin, Rutin, Metformin.

Author contributions: Conceptualization, Sunday N Okafor, Oluebube Amanda Ekworomadu and Chinelo Obianuju Nwinyi; Methodology, Sunday N Okafor, Oluebube Amanda Ekworomadu and Chinelo Obianuju Nwinyi; Software, Sunday N Okafor; Investigation, Oluebube Amanda Ekworomadu and Chinelo Obianuju Nwinyi; Writing - original draft, Oluebube Amanda Ekworomadu; Writing - review and editing, Sunday N Okafor; Visualization, Sunday N Okafor, Oluebube Amanda Ekworomadu and Chinelo Obianuju Nwinyi; Supervision, Sunday N Okafor; Project administration, Sunday N Okafor;



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Sciforum-210380: Design, synthesis, and biological evaluation of imidazophenanthrolines as human topoisomerase I inhibitors

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Cancer remains one of the major health challenges worldwide, highlighting the need for new and more effective therapeutic strategies. Among the molecular targets identified for cancer therapy, human topoisomerase I (TOP1) is a clinically validated target. The camptothecin (CPT) derivatives irinotecan and topotecan exert their antitumoral activity by targeting TOP1. However, despite their clinical efficacy, these drugs present important limitations, including severe side effects, the development of resistance, and the instability of the pharmacologically active lactone ring under physiological conditions. Therefore, the development of novel, structurally CPT-unrelated TOP1 inhibitors represents a promising strategy for anticancer drug discovery.

CPT derivatives and several other reported TOP1 inhibitors share a common structural feature consisting of a planar polycyclic core with an extended π-conjugated system. Based on these characteristics, we designed a series of imidazophenanthrolines and evaluated their potential as TOP1 inhibitors.

Herein, we report the synthesis and characterization of these compounds together with their biological evaluation. DNA relaxation assays revealed an irreversible TOP1 inhibition profile, in contrast to the reversible mode of action displayed by CPT. Moreover, the compounds showed promising antiproliferative activity against A549 lung carcinoma cells, with IC_{50} values ranging from the low micromolar to the nanomolar range. Evaluation of selective toxicity towards lung carcinoma cells further identified several compounds displaying greater selectivity than the reference compound CPT.

Overall, these results support imidazophenanthrolines as promising scaffolds for the development of novel CPT-unrelated TOP1-targeting anticancer agents.



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Sciforum-210398: Novel respiratory syncytial virus replication inhibitors based on monoterpene conjugates and 3-substituted 7-hydroxycoumarins

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Respiratory syncytial virus (RSV) causes respiratory infections, leading to annual epidemics in the cold seasons. It is especially dangerous for infants and the elderly.

Coumarin and its derivatives have a wide range of pharmacological properties, including antitumor, antibacterial and antiviral activity, as well as anti-HIV, anti-inflammatory and anticoagulant properties.

Significant progress in recent decades has been made in identifying potential targets for RSV therapy and in the search for small molecule inhibitors of RSV replication. Thus, 7-hydroxycoumarins monoterpene conjugates containing various substituents at C-4 position of the coumarin scaffold proved to be effective. Later it was suggested that the use of their analogues with substituents at C-3 position of the coumarin backbone may be promising for RSV replication inhibition, based on molecular docking to RSV protein F as molecular target which is responsible for virus entry into the host cell [1].

In this work we synthesized the first eighteen conjugates of C-3 substituted 7-hydroxycoumarins, thus developed and optimized methods for the synthesis of these compounds. Among the synthesized compounds, agents demonstrating promising anti-RSV activity with IC_{50} in the lower micromolar range were found. The compounds are most active in the early stages of infection, apparently preventing the virus from entering the cell by binding to the F RSV protein.1. Khomenko, T. M.; Shtro, A. A.; Galochkina, A. v.; Nikolaeva, Y. v.; Garshinina, A. v.; Borisevich, S. S.; Korchagina, D. v.; Volcho, K. P.; Salakhutdinov, N. F. New Inhibitors of Respiratory Syncytial Virus (RSV) Replication Based on Monoterpene-Substituted Arylcoumarins. *Molecules* **2023**, *28* (6), 2673. https://doi.org/10.3390/molecules28062673.

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Sciforum-210410: Molecular Docking Analysis of Selected Thiourea Derivatives of Naproxen with Human Serum Albumin

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Human serum albumin (HSA) plays a key role in the transport and distribution of numerous drugs, including nonsteroidal anti-inflammatory agents. Naproxen, a widely used propionic acid derivative, exhibits extensive binding to HSA, while structural modification of its molecular scaffold may alter its protein-binding properties. In our previous study, the binding of 14 newly synthesized thiourea derivatives of naproxen to HSA was experimentally investigated using high-performance affinity chromatography (HPAC). Based on the experimentally determined binding affinities, four derivatives were selected for further *in silico* analysis, comprising two compounds with high affinity (**8** and **12**) and two with low affinity (**13** and **14**), while naproxen was included as a reference ligand. The target enzyme and ligand conformations were prepared using MAKE Receptor and OMEGA, respectively, followed by molecular docking with the FRED tool of OEDocking. The resulting ligand-HSA complexes were evaluated based on docking scores and non-covalent interactions. Compounds **8** and **12** exhibited the most favorable docking scores (-12.50 and -12.66 kcal/mol, respectively), surpassing that of naproxen (-9.71 kcal/mol), and formed multiple hydrogen-bonding, hydrophobic, and π-interactions with residues within the HSA binding site. In contrast, compounds **13** and **14** showed substantially less favorable docking scores (-7.94 and -7.30 kcal/mol, respectively) and distinct interaction patterns. Overall, the docking results were consistent with the experimentally determined affinity-based selection of the compounds, supporting the applicability of molecular docking for providing molecular-level insights into the HSA-binding behavior of thiourea derivatives of naproxen.



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Sciforum-210466: Synthesis and in vitro/in silico antitumor evaluation of 4-sulfanylquinolinyl amide derivatives

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The contemporary understanding of cancer in 2026 defines it as a systemic and multifactorial breakdown of biological homeostasis, characterized by a profound dysregulation of the molecular signaling networks that govern cell growth, survival, and differentiation. Although therapeutic management remains anchored in surgery, radiotherapy, and chemotherapy, chemoresistance persists as a critical obstacle, driving the search for new antineoplastic agents. This study reports the synthesis and structural characterization (via IR and NMR) of novel 4-sulfanylquinolinyl amide derivatives and their intermediates, as well as their *in vitro* and *in silico* antitumor biological evaluation. Preliminary cytotoxicity assays were conducted against the chronic myeloid leukemia cell line (K562) for intermediates **3** and **4** and the final products **6a–f**. The compounds demonstrated moderate antiproliferative activity. Intermediate **4** (IC_{50} = 15.41 µM) and the final product **6f** (IC_{50} = 19.65 µM) exhibited superior efficacy compared to the commercial control, quercetin (IC_{50} = 24.75 µM). Furthermore, *in silico* predictions of the ADME profile suggest favorable pharmacokinetic properties and good compliance with oral bioavailability criteria. These findings position 4-sulfanylquinolinyl amides as promising lead structures for the design and optimization of future chemotherapeutic drugs.

Author contributions: Conceptualization, Zuleyma Blanco Marquez and Jaime Enrique Charris; Methodology, Zuleyma Blanco Marquez, Andrea Katherina Delgado and Jaime Enrique Charris; Validation, Zuleyma Blanco Marquez and Jaime Enrique Charris; Formal analysis, Zuleyma Blanco Marquez; Investigation, Zuleyma Blanco Marquez, Andrea Katherina Delgado and Jaime Enrique Charris; Resources, Zuleyma Blanco Marquez; Writing - original draft, Zuleyma Blanco Marquez; Writing - review and editing, Zuleyma Blanco Marquez and Jaime Enrique Charris; Visualization, Jaime Enrique Charris; Supervision, Zuleyma Blanco Marquez and Jaime Enrique Charris; Project administration, Zuleyma Blanco Marquez;



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Sciforum-210473: Synthesis of new derivatives of 8-trifluoromethylquinobenzothiazine

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Phenothiazine is an important heterocyclic scaffold present in numerous biologically active compounds. Its derivatives exhibit a broad spectrum of pharmacological activities, including anticancer, antibacterial, antiviral, antifungal and anti-inflammatory effects. Due to their diverse biological properties, phenothiazine derivatives have been the subject of our previous studies, particularly in the search for compounds with antiproliferative and antibacterial activity. The present study is a continuation of our previous research on 8-trifluoromethylquinobenzothiazine derivatives. The aim of this study was to synthesize new derivatives of 8-trifluoromethylquinobenzothiazine for further investigation of their biological properties. The synthesis was carried out using two synthetic pathways. The first path consisted of reaction between 8-trifluoromethylquinobenzothiazine and *N*-(4-bromobutyl)phthalimide that led to obtaining butylphthalimide derivative. Then that derivative underwent hydrolysis with hydrazine hydrate in ethanol to 6-aminobutyl-8-trifluoromethylquinobenzothiazine. The 6-aminobutyl-8-trifluoromethylquinobenzothiazine was use to synthesize six different derivatives: acetylaminobutyl, metanosulfonylbutyl, *p*-tolylsulfonylbutyl, chloroethylureidobutyl, *p*-trifluoromethylureidobutyl and *p*-tolylsulfonylureidobutyl. The second path included reaction between 8-trifluoromethylquinobenzothiazine and 1-bromo-4-chlorobutane that resulted in getting chlorobutyl derivative. The chlorobutyl derivative was then use to synthesize four different derivatives: 1-methylpiperazinylbutyl, 1-(2-hydroxyethyl)piperazinylbutyl, 1-phenylpiperazinylbutyl and 1-pyridinylpiperazinylbutyl. The structure of all synthesized compounds was confirmed by spectroscopic analysis such as ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and mass spectrometry ESI HRMS. The applied synthetic approaches proved effective for the preparation of new 8-trifluoromethylquinobenzothiazine derivatives and provided a series of compounds suitable for further evaluation of their biological activity.



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Sciforum-210510: Dual-target pyrrolo[1,2-a]quinoxaline hydrazones : bridging anti-leukemic and antimalarial drug discovery

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This study reports the synthesis, structural characterization and evaluation of new pyrrolo[1,2-*a*]quinoxaline-2-carboxylic acid hydrazone derivatives (**1a–1f**) as structural analogues of the antileukemic reference compounds HY-143278 and NVX-412, and synthesized from 2-nitroaniline through a six-step pathway. Structural characterization was achieved by $^{1}H/^{13}C$ NMR, HRMS, and single-crystal X-ray diffraction (for **1c**, **1d**, and **1f**), confirming the (*E*)-configuration of the hydrazone linkage and, for **1d**, a minor ketoenol tautomeric equilibrium in solution.

These compounds were first evaluated *in vitro* against the human acute myeloid leukemia cell line MV4-11 (FLT3-ITD mutated). Only the pyridin-2-yl derivative **1a** showed measurable antiproliferative activity (IC_{50} = 15.51 µM), with low toxicity toward healthy hFF-1 fibroblasts (selectivity index $>$ 3.22). Given the structural similarity between hydrazones **1**and a recently reported antimalarial quinoline-hydrazone, the series was further screened for antiplasmodial activity against the chloroquine-sensitive (3D7) and chloroquine-resistant (W2) strains of *Plasmodium falciparum*. The pyridin-4-yl derivative **1c** displayed the highest potency against 3D7 (IC_{50} = 0.02 µM, SI $>$ 5000), while the pyrimidinyl derivative **1e** was the most active against W2 (IC_{50} = 0.03 µM, SI $>$ 3333) both markedly outperforming chloroquine's selectivity profile. None of the compounds showed cytotoxicity toward human HepG2 hepatic cells (CC_{50} $>$ 100 µM), and the ferrocenyl analogue **1f** was unexpectedly inactive against both parasitic strains.

Overall, these results demonstrate that subtle structural modifications of the pyrrolo[1,2-*a*]quinoxaline-hydrazone scaffold drive distinct and selective biological profiles, positioning this chemical series as a versatile platform bridging anti-leukemic and antimalarial drug discovery.

Author contributions: Conceptualization, Jean Guillon; Methodology, Jean Guillon and LARI Lindita; Validation, Jean Guillon; Formal analysis, LARI Lindita; Investigation, Jean Guillon and LARI Lindita; Writing - original draft, Jean Guillon; Writing - review and editing, Jean Guillon; Visualization, Jean Guillon and LARI Lindita; Supervision, Jean Guillon; Project administration, Jean Guillon; Funding acquisition, Jean Guillon;



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Sciforum-210515: Novel Glycosylpyrazoles as Tumour-Associated Carbonic Anhydrase Inhibitors: Key Roles of Sulfonamide and Methoxyaryl Groups in Isoform Selectivity

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Hypoxic tumour microenvironments overexpress transmembrane human carbonic anhydrases IX and XII (*h*CA IX and XII), metalloenzymes that feature a Zn^{2+} ion at their active sites and play key roles in pH regulation, tumour survival, and metastasis. Selective inhibition of these tumour-associated isoforms over widespread cytosolic isoforms *h*CA I and II represents an attractive strategy for targeted cancer therapy.

Herein, we report the rational design and synthesis of a novel family of sulfonamide-functionalized glycosyl pyrazoles incorporating D-glucose and D-galactose scaffolds. The synthetic route involves constructing key glycosyl isoxazolines intermediates via 1,3-dipolar cycloaddition, followed by ring opening and oxidation to afford glycosyl-β-diketones, which are subsequently cyclized with 4-hydrazinobenzenesulfonamide to yield 1,5-disubstituted pyrazoles. Inhibitory activities (*Ki*) against *h*CA I, II, IX and XII were evaluated using a stopped-flow CO_2 hydration assay.

The synthetised glycoconjugates displayed potent nanomolar inhibition against tumour-associated isoforms *h*CA IX (*Ki* values as low as 54.6 nM) and *h*CA XII (*Ki* values as low as 32.4 nM). Comparative assays confirmed that the sulfonamide group is essential for Zn^{2+} coordination and enzyme inhibition. Incorporation of an aromatic methoxy substituent substantially decreased affinity for cytosolic *h*CA I, thereby significantly improving isoform selectivity, with selectivity ratios of up to 165-fold for *h*CA I over *h*CA XII.

These findings demonstrate that these novel glycosyl pyrazoles represent promising scaffolds for the development of targeted anticancer agents. Ongoing work is focused on evaluating their cellular activity in osteosarcoma cell lines under normoxic and hypoxic conditions, aiming to further validate their efficacy in 3D spheroid models.

Author contributions: Conceptualization, Pedro Alfonso Colinas; Methodology, Ivan Alejandro Barri; Investigation, Ivan Alejandro Barri; Resources, Pedro Alfonso Colinas; Writing - original draft, Ivan Alejandro Barri; Writing - review and editing, Ivan Alejandro Barri and Pedro Alfonso Colinas; Supervision, Pedro Alfonso Colinas; Project administration, Pedro Alfonso Colinas; Funding acquisition, Pedro Alfonso Colinas;



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Sciforum-210608: In Silico and *In Vitro* Evaluation of Novel Fiscalin Derivatives as P-Glycoprotein Modulators for Alzheimer's Disease

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Alzheimer's disease (AD) is a neurodegenerative disorder characterized by amyloid-beta (Aβ) accumulation in the brain. Central nervous system homeostasis is maintained, in part, by the blood-brain barrier (BBB), where the luminal efflux transporter P-glycoprotein (P-gp/ABCB1) plays a key role in clearing Aβ into the systemic circulation. In AD, BBB impairment and the loss of P-gp function disrupt this mechanism, accelerating Aβ deposition, neuroinflammation, and cognitive decline [1]. Fiscalins are valine-derived alkaloids bearing an indolyl moiety and a tricyclic anthranilic acid scaffold, previously reported to modulate P-gp activity and exert neuroprotective effects [2]. This work thus aimed to elucidate, *in silico*, the P-gp binding sites of 10 new synthetic fiscalin derivatives (FDs), using Molecular Operating Environment (MOE) and AutoDock Vina software, and to evaluate, *in vitro*, their cytotoxicity (0-50 µM; neutral red uptake and MTT reduction assays; 24 h exposure) and their effects on P-gp activity (rhodamine 123 [Rho123] accumulation assay) in differentiated SH-SY5Y cells. Docking analysis revealed that all FDs bound to P-gp at three binding sites: the drug-binding pocket (DBP) and nucleotide-binding domains (NBDs) 1 and 2. Within the DBP - a typical substrate-binding site - FDs displayed lower (more negative) binding energies than known P-gp substrates, indicating higher affinity. They preferentially occupied the modulator (M) site, except FD5.1, whose lowest binding energy occurred at the Rho123 site. *In vitro*, FD2-FD6.1 were non-cytotoxic at concentrations up to 25 µM, FD6.2 and FD7 were safe up to 10 µM, and FD1 only at 5 µM. Notably, FD1 and FD4 significantly enhanced P-gp activity, suggesting an increased capacity to efflux substrates across the BBB. Given the role of P-gp in Aβ clearance, these findings identify FDs as a novel chemical scaffold for restoring BBB efflux function, opening a promising avenue for disease-modifying strategies in AD.



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Sciforum-210721: Molecular Docking Investigation of Eg5 Enzyme Inhibition by Hydroxyquinolone Derivatives

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Kinesin spindle protein (KSP), also known as Eg5, is a member of the kinesin superfamily of molecular motor proteins that utilize the energy generated by ATP hydrolysis to facilitate the transport and organization of microtubules and other intracellular components. KSP plays a crucial role in the formation and maintenance of the bipolar mitotic spindle and is therefore considered an attractive molecular target for anticancer drug development. Since the discovery of Monastrol in 1999, numerous KSP inhibitors have been identified and investigated. Most reported KSP inhibitors are ATP-uncompetitive allosteric inhibitors that reversibly inhibit the ATPase activity of Eg5 and encompass a wide range of structural classes. In the present study, hydroxyquinolone derivatives, which are known for their broad range of pharmacological activities, including anticancer, and anti-inflammatory properties, were investigated as potential Eg5 inhibitors. Molecular docking studies were performed to evaluate the binding modes and predicted affinities of the investigated derivatives toward the Eg5 binding site. All compounds exhibited favorable docking scores ranging from -6.92 to -7.02 kcal/mol, indicating their potential to establish stable interactions with the enzyme. The most favorably ranked derivatives were accommodated within the active binding pocket through hydrogen bonding, hydrophobic contacts, and other stabilizing interactions. In particular, the hydroxyl groups present in the hydroxyquinolone scaffold appeared to contribute to ligand recognition and binding stabilization through hydrogen bonding interactions with key amino acid residues.

Author contributions: Conceptualization, Abdeslem Bouzina; Software, Ikram Zerguine ; Investigation, Rachida Mansouri; Writing - original draft, Abdeslem Bouzina; Writing - review and editing, Rachida Mansouri;



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Sciforum-210734: In vivo genotoxic and antigenotoxic effects of a selected pyrazole-chromeno[2,3-d]pyrimidine derivative in Wistar rats

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Pyrazole-chromeno[2,3-d]pyrimidine derivatives are heterocyclic compounds with diverse biological activities and potential as bioactive small molecules. Following multistep screening of eight derivatives, 8,9-dihydroxy-5-(5-methyl-3-oxo-2,3-dihydro-1H-pyrazol-4-yl)-1,5-dihydro-2H-chromeno[2,3-d]pyrimidine-2,4(3H)-dione (PCP-4) was selected for further investigation of its DNA-protective potential, based on its in vitro DNA-protective activity and in vivo antigenotoxic effects in Drosophila melanogaster. Its in vivo genotoxic and antigenotoxic effects were evaluated in the liver of male Wistar rats using the alkaline comet assay. Eight groups (n = 5/group; 8-10 weeks old; approximately 250 g) received 0.9% NaCl intraperitoneally as the negative/vehicle control, EMS alone (300 mg/kg), PCP-4 alone (1.25, 2.5, or 5 mg/kg), and PCP-4 administered 24 h after EMS treatment. Animals were sacrificed 24 h after PCP-4 administration, and liver samples were collected for DNA damage assessment. PCP-4 at 1.25 mg/kg did not significantly increase DNA damage, whereas 2.5 and 5 mg/kg produced moderate but significant increases. Total comet scores for PCP-4 alone were 23.10 ± 0.41, 40.60 ± 0.49, and 45.00 ± 1.00, respectively, compared with 166.30 ± 0.17 for EMS alone. Although higher PCP-4 doses showed intrinsic genotoxicity, the magnitude of DNA damage remained markedly lower than that produced by EMS under these conditions. Post-treatment with PCP-4 significantly reduced EMS-induced DNA damage by 82.3%, 80.1%, and 69.3%, respectively. These findings reveal a dose-dependent dual response, with pronounced antigenotoxic activity at lower doses and increased intrinsic genotoxicity at higher doses. Further studies are needed to determine the optimal protective dose of PCP-4 and elucidate the mechanisms underlying its dose-dependent effects.



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Sciforum-210802: Design, Synthesis and Biological Evaluation of 2-Methylthieno[2,3-d]pyrimidine Derivatives as Potential Cognitive-Modulating Agents

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Cognitive impairment is a characteristic feature of neurodegenerative disorders and remains an important challenge in drug discovery. Thienopyrimidines represent a promising class of heterocyclic compounds with diverse biological activities and potential applications in the development of CNS-active agents. In this study, a series of 2-methylthieno[2,3-d]pyrimidin-4(3H)-one derivatives bearing an acetamide fragment at position 3 was designed, synthesized, and evaluated as potential cognitive-modulating agents.

The synthesized compounds were characterized by spectroscopic and analytical methods and subjected to in silico ADMET profiling. Molecular docking was performed to investigate their potential interactions with acetylcholinesterase (AChE) and the NMDA receptor, two targets involved in cognitive function. The derivatives demonstrated favorable predicted interactions with both targets, and compounds 4d and 4e were selected for extended biological evaluation.

The compounds were evaluated in a scopolamine-induced model of cognitive impairment in mice. Behavioral assessment included the Passive Avoidance Test, Open Field Test, Rotarod Test, Novel Object Recognition Test, and Morris Water Maze. Initial screening identified derivatives 4d and 4e as the most active representatives of the series. Among them, compound 4e demonstrated the most consistent behavioral effects, improving recognition memory and spatial learning and memory without evidence of generalized locomotor stimulation.

Overall, compound 4e was identified as a promising lead within this thieno[2,3-d]pyrimidine series, supporting further medicinal chemistry optimization and mechanistic investigation.



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Sciforum-210805: Synthesis of tetraketones and determination their biological activity

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Tetraketones are cyclic compounds, synthetised from dimedone (cyclohexane-1,3-dione) and benyaldehydes via Knoevenegel condenzation and Michaels addition, by principles of green chemistry with catalyst. They are very interesting because they have wide range of biological activity such as antioxidant activity and inhibitory activity against enzymes lopoxygenase, tyrosinase and protein kinase. It has been determined that have strong cytotoxic as well as antimicrobial activity. The primary aim of this study was to synthesize new series of tetraketones and to relate their biologcal activity to chemical structure. Results showed that all synthesized tetraketones have different antioxidant activity, compounds with hydroxyl group in the structure were responsible for the strongest activity, also we found the correlation between the number of gropus and activity. Compound with ortho hydroxyl groups in the phenyl ring proved to be strongest antioxidant and has stronger activity than vitamin C. They also act as strong inhibitors of the enzyme tyrosinase, the most potent compound is with ortho hydroxyl groups in the ring, at the concentration of 512 μM inhibits tyrosinase activity of 86,9%, other compounds show weaker inhibitory activity. Stronger antimicrobial activity have compounds with lipophilic aromatic substituents, SAR analysis suported by SwissADME parameters indicated that the observed antimicrobial activity deepends on balanced relationship between lipophilicity, polarity and diffusion properties of the molecules. There is a correlation between biological activity and structure of tetraketones, compounds with polar funcional groups such as hydroxy, methoxy and ethoxy have stronger antioxidant activity and inhibitory activity against tyrosinase; compounds with lipophilic substituents such as fluorine, chlorine and trifluoromethly have better antimicrobial activity.

Author contributions: Methodology, Amra Džambić, Maida Šljivić Husejnović and Demir Bjelošević; Software, Amra Džambić and Demir Bjelošević; Validation, Maida Šljivić Husejnović ; Formal analysis, Darja Husejnagić and Emir Horozić; Writing - original draft, Amra Džambić and Ajla Begić; Writing - review and editing, Demir Bjelošević; Supervision, Samija Muratović;



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Sciforum-210822: Synthesis, Structural Characterization and Biological Activity of Silver(I) Complexes with 1-Phenylimidazole

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Silver(I) complexes have attracted considerable attention in coordination and medicinal chemistry due to their pronounced antibacterial and antifungal properties. In this study, two silver(I) complexes with 1-phenylimidazole (phim), $[Ag(phim)_2]SbF_6$ (**Ag1**) and $[Ag(phim)_2]BF_4$ (**Ag2**), were synthesized by reacting the corresponding AgX salts (X = SbF_6^- and BF_4^-) with the phim ligand in a 1 : 1 molar ratio in ethanol at room temperature in the absence of light. The synthesized silver(I) complexes were characterized by elemental analysis, molar conductivity measurement, ^{1}H NMR, IR, and UV-Vis spectroscopy, and cyclic voltammetry, while their crystal structures were determined by single crystal X-ray diffraction. In both complexes, two phim ligands are coordinated to the Ag(I) center in a monodentate fashion through the N3 atom of the imidazole ring, forming the cationic $[Ag(phim)_2]^+$ species, which is charge-balanced by the corresponding counter-anion. The antimicrobial activity of complexes **Ag1** and **Ag2** was evaluated against a panel of bacterial and fungal strains, while their cytotoxicity was assessed using the normal human lung fibroblast cell line (MRC-5). *In vitro* biological assays demonstrated that both silver(I) complexes exhibit good to moderate antibacterial and antifungal activities. Notably, coordination of 1-phenylimidazole to Ag(I) enhanced its antimicrobial activity compared with the free ligand. These findings highlight the potential of silver(I) complexes containing *N*-heterocyclic ligands as promising candidates for the development of novel antimicrobial agents.

Author contributions: Conceptualization, Nevena Lj. Stevanović and Biljana Đ. Glišić; Methodology, Nevena Lj. Stevanović, Tina P Andrejević and Bojana Vučko Pantovic; Software, Jakob Kljun; Validation, Darko Asanin; Investigation, Sanja Bogojevic, Darko Asanin and Tina P Andrejević; Resources, Sanja Bogojevic and Biljana Đ. Glišić; Writing - original draft, Nevena Lj. Stevanović; Visualization, Jakob Kljun and Bojana Vučko Pantovic; Supervision, Biljana Đ. Glišić;



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Sciforum-210845: Mpro-Targeting Small Molecules and PROTACs with SARS-CoV-2 vs HCoV-OC43 Selectivity

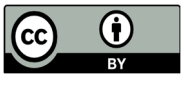
Fausta Ulgheri [1,*], Giovanni Loriga [1], Andrea Beccu [1], Antonio Dore [2], Giuseppina Sanna [3], Luca Virdis [3] and Pietro Spanu [1]

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Coronaviruses remain a major global health threat, highlighting the need for broad-spectrum antiviral agents effective against both circulating and emerging viral pathogens. The structural and functional conservation of the main protease (Mpro) across coronaviruses makes it an attractive target for broad-spectrum antiviral development. Herein, we report the design, MCR-based synthesis, and biological evaluation of a novel class of non-covalent, non-peptidic Mpro-targeting compounds and their corresponding PROTACs derivatives as antivirals candidates against coronaviruses infections. Starting from a fragment-based drug discovery approach, a series of small molecules was designed and synthesized one-pot via a Ugi four-component reaction (U-4CR). The compounds were evaluated for SARS-CoV-2 Mpro inhibition and antiviral activity in cellular models. The most active compound inhibited Mpro and showed antiviral activity against SARS-CoV-2 in the low-micromolar range, with no cytotoxicity. Notably, a closely related analogue differing by only one methyl group displayed complementary antiviral activity against HCoV-OC43 while being inactive against SARS-CoV-2, although enzymatically inhibiting Mpro albeit with reduced potency. This divergent profile was retained in the corresponding PROTAC derivative, which inhibited HCoV-OC43 replication with the same low micromolar EC_{50} but showed no measurable activity against SARS-CoV-2. Overall, these results demonstrate antiviral activity against two distinct human coronaviruses within a closely related series of Mpro-targeting compounds, supporting these compounds as a promising starting point for the development of pan-coronavirus antivirals. Structure-activity relationship (SAR) studies are underway to optimize antiviral potency and broaden the spectrum of activity to other coronaviruses beyond the two studied so far.

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Sciforum-210928: Structure-Based Discovery and Prioritization of Selective Tryptophan Hydroxylase 1 Inhibitors through Drug Repurposing for Hepatocellular Carcinoma

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TPH1 is the rate-limiting enzyme responsible for peripheral serotonin biosynthesis. TPH1 is an established therapeutic target for several serotonin-associated disorders and has emerged as a novel drug target to treat hepatocellular carcinoma. However, its high structural similarity to other aromatic amino acid hydroxylases presents a major challenge in the development of TPH1-specific therapeutics. The current study employed an integrative structure-based drug-repurposing strategy to identify selective TPH1 inhibitors through computational selectivity profiling against closely related paralogous enzymes.

Four experimentally determined structures of human TPH1, representing distinct inhibitor-binding pockets, were used to screen potential inhibitors against FDA-approved and investigational drugs from commercial drug competitive intelligence databases. The docking protocol was validated by successfully docking the co-crystallized ligands before conducting high-throughput virtual screening and Glide Standard Precision docking with the Schrodinger suite. Top-ranked compounds were subsequently subjected to selectivity profiling against paralogous enzymes, followed by Prime MM/GBSA binding free-energy calculations to prioritize selective TPH1 binders. Molecular dynamics simulations of the candidate hits revealed variable ligand-binding stability, emphasizing the importance of receptor flexibility in accurate binding-mode prediction. To account for receptor flexibility and further refine ligand-binding conformations, induced fit docking studies are currently in progress. Collectively, the study identified promising candidate compounds with potential TPH1 selectivity, providing a foundation for further structural optimization and experimental validation toward the development of TPH1-targeted therapeutics for HCC.

Author contributions: Conceptualization, V S Vidya; Methodology, V S Vidya and Saravanan Parameswaran; Software, V S Vidya; Validation, V S Vidya, Sahana H and Saravanan Parameswaran; Formal analysis, V S Vidya, Sahana H and Saravanan Parameswaran; Investigation, V S Vidya and Saravanan Parameswaran; Resources, V S Vidya; Data curation, V S Vidya; Writing - original draft, V S Vidya; Writing - review and editing, V S Vidya, Sahana H and Saravanan Parameswaran; Visualization, V S Vidya; Supervision, Saravanan Parameswaran;



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Sciforum-210930: From Metabolome to Molecule: Discovery of Bioactive Small-Molecule Drug Candidates from *Cupressus torulosa D. Don*

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Cupressus torulosa D. Don is an underexplored Himalayan conifer with potential as a source of bioactive natural products and a history of ethnopharmacological use for inflammatory conditions. This study integrates metabolomics, pharmacological evaluation, and molecular docking to identify and prioritize bioactive small molecules from *C. torulosa* needles. **25% methanolic needle extracts** were subjected to LC-QTOF-MS/UPLC-QTOF-MS profiling and chemometric analysis to characterize metabolite diversity and identify potentially important constituents. **The extracts were evaluated *in vitro* for antioxidant, α-amylase/α-glucosidase inhibitory and albumin-denaturation activities, and *in vivo* for anti-inflammatory and antidiabetic effects using paw-edema and streptozotocin-induced models, respectively.** Based on their occurrence, bioactivity and pharmacological relevance, **amentoflavone and fraxin** were selected for molecular docking studies against therapeutically relevant targets, including **α-amylase, α-glucosidase, COX-2 and 5-LOX**. The integrated approach revealed diverse phenolic compounds, flavonoids, terpenoids and other metabolites with promising biological activities. These findings demonstrate the potential of *C. torulosa* as a source of natural-product-derived bioactive molecules and provide a metabolome-to-molecule framework for lead prioritization and future drug-discovery studies.

Author contributions: Conceptualization, Radhika Khanna; Methodology, Radhika Khanna; Software, Radhika Khanna; Validation, Radhika Khanna; Formal analysis, Radhika Khanna; Writing - original draft, Radhika Khanna; Writing - review and editing, Radhika Khanna; Visualization, Radhika Khanna; Supervision, Radhika Khanna; Project administration, Radhika Khanna;



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Sciforum-210978: Metallodrug-Protein Interactions at Physiological Temperature: Structural Insights from X-ray Crystallography at 37 °C

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Protein metalation is a fundamental biological process through which proteins interact with metal ions or complexes, leading to the formation of stable metal–protein adducts. Understanding protein metalation under physiologically relevant conditions is essential for gaining deeper insights into the mechanisms of action of metallodrugs. Temperature is a key factor that can affect metal coordination geometry, ligand exchange processes, and protein conformational flexibility. Therefore, structural studies performed at physiological temperature can provide a more representative picture of metal–protein interactions in biological systems.

We have developed an experimental protocol for the growth of crystals of adducts formed upon reaction of metallodrugs with proteins at 37 °C and for the collection of X-ray diffraction data at the same temperature. X-ray structures of the adducts formed by the model protein hen egg white lysozyme (HEWL) with bis(acetylacetonato)oxidovanadium(IV), [$V^{IV}O(acac)_2$], and dirhodium tetraacetate, [$Rh_2(\mu\text{-}O_2CCH_3)_4$] were obtained and solved. Then, the resulting structures were compared with those previously determined at cryogenic temperature (100 K). At 37 °C, the reaction of [$V^{IV}O(acac)_2$] with HEWL results in the formation of polyoxidovanadate (POV) clusters whose structural features differ markedly from those observed at 100 K. In contrast, the structure of the [$Rh_2(\mu\text{-}O_2CCH_3)_4$]/HEWL adduct at 37 °C remains largely comparable to that determined at 100 K, with differences mainly involving metal occupancy and local residue mobility.

Overall, these findings highlight the significant influence of temperature on metal coordination and speciation in metal–protein systems and demonstrate the importance of performing structural investigations at physiological temperature to obtain a more realistic description of metallodrug–protein interactions and their potential biological behaviour.



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Sciforum-210981: Structural characterization of vanadium binding to human serum transferrin

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Human serum transferrin (hTF), the major iron-transport protein in blood, can also interact with non-Fe ions and with metal compounds of medicinal interest, potentially influencing their distribution and biological activity.[1] Vanadium compounds have attracted considerable interest for their pharmacological properties, although the molecular consequences of their interaction with hTF are not fully understood.[2] Recently, crystallographic studies provided the first evidence at atomic level of vanadium binding to a monoferric form of hTF.[3]

Here, the interaction between the apo form of hTF and the potential metallodrug $[V^{IV}O(acac)_2]$ was investigated by X-ray crystallography and urea-polyacrylamide gel electrophoresis (Urea-PAGE). Crystals obtained by co-crystallization after 24 and 48 h of incubation revealed the formation of divanadate(V) species. Two $[V^{V}_2O_6]^{2-}$ anions were identified within the Fe^{3+} binding sites coordinated to Tyr188 and Tyr517, respectively. Notably, vanadium binding to Tyr517 had not been previously reported.

Despite occupation of the Fe^{3+}-binding sites, structural analysis showed that hTF retains the NopenCopen conformation characteristic of its apo form, indicating that divanadate(V) binding does not induce the conformational rearrangements typically associated with Fe^{3+} binding. Urea-PAGE experiments confirmed that this occurs also in solution.

Thus, hTF binds divanadate(V) species within iron-binding sites without undergoing the conformational transition associated with efficient transferrin receptor recognition. These findings provide molecular insights into vanadium–transferrin interactions and support a limited contribution of vanadium(V)-bound hTF to cellular vanadium uptake through receptor-mediated endocytosis.

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Sciforum-210991: Influence of the aromatic substituent on the α-glucosidase inhibitory activity of D-ribose derived 1,2,3-triazoles

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International Diabetes Federation estimates that 1 in 9 adults aged 20-79 years is living with diabetes; more than 90% of these cases correspond to type 2 diabetes.[1] One therapeutic strategy for controlling postprandial hyperglycemia is the inhibition of α-glucosidase. Most known α-glucosidase inhibitors are glycomimetics that resemble the natural substrates of the enzyme, which facilitates their binding to the active site. Among them, carbohydrate-derived 1,2,3-triazoles have previously been reported as α-glucosidase inhibitors.[2]

On this basis, a new set of D-ribose-derived triazoles was synthesized and characterized. These compounds were designed to share the same carbohydrate-triazole core while differing only in the aromatic substituent. D-Ribose was protected as its 2,3-*O*-isopropylidene methyl glycoside leaving a free hydroxyl group at C-5. The protected sugar was then converted into the corresponding tosylate, which underwent nucleophilic displacement with azide to afford the 1,3-dipole. The dipolarophiles were prepared by *O*-propargylation of the corresponding phenols or benzyl alcohol with propargyl bromide. The target compounds were obtained in high yields through CuAAC reaction of both precursors in water/dichloromethane, using copper(II) sulfate and sodium ascorbate as the catalytic system.

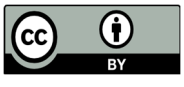
All products were evaluated against maltase from *Saccharomyces cerevisiae* and murine α-glucosidase following previously reported procedures.[3] The most active compound, derivative of pentafluorophenol, showed an IC_{50} value of 25.63 μM, comparable to that of the reference inhibitor quercetin (IC_{50} = 20 μM), while showing only slight inhibition of the murine enzyme (around 10%). The rest of the synthesized compounds showed negligible inhibition of the enzyme, with an IC_{50} $>$ 500 μM.

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Author contributions: Conceptualization, Pedro Alfonso Colinas; Investigation, Ignacio Aznar and Macarena Soledad Le Pors; Writing - original draft, Ignacio Aznar; Writing - review and editing, Macarena Soledad Le Pors and Pedro Alfonso Colinas; Supervision, Macarena Soledad Le Pors and Pedro Alfonso Colinas; Project administration, Pedro Alfonso Colinas; Funding acquisition, Pedro Alfonso Colinas;



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Sciforum-211021: In silico identification of EGFR tyrosine kinase inhibitors for glioblastoma

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Glioblastoma (GBM) is the most common malignant primary brain tumor in adults and is characterized by rapid progression, limited therapeutic options and poor survival outcomes. Aberrant activation of receptor tyrosine kinases (RTKs), particularly epidermal growth factor receptor (EGFR), results in persistent activation of oncogenic signalling pathways promoting tumorigenesis, disease progression and therapeutic resistance. Although several RTK inhibitors have been evaluated in clinical trials for GBM, their therapeutic efficacy remains limited by challenges such as the development of drug resistance and low blood-brain barrier (BBB) penetration. This study aimed to identify potential EGFR tyrosine kinase inhibitors using various *in silico* methods. Ligand-based virtual screening of chemical databases was performed using the SwissSimilarity web tool, applying a combined 2D-fingerprint and 3D-shape similarity search algorithm. Lapatinib, a dual EGFR/HER2 tyrosine kinase inhibitor that binds to the inactive-like conformation of EGFR kinase domain, was used as the reference ligand for similarity searching. A total of 688 structural analogs of lapatinib were subsequently retrieved and evaluated for physicochemical properties, pharmacokinetic parameters, drug-likeness and toxicity using SwissADME and ProTox 3.0 web servers. A subset of 16 compounds exhibiting favorable predicted pharmacokinetic and safety profiles, BBB penetration and drug-like characteristics were prioritized for molecular docking. Molecular docking was performed using AutoDock Vina to estimate the binding affinities of selected compounds to the target protein. Predicted binding poses and molecular interactions were visualized using PyMOL. Molecular docking revealed several compounds with favorable binding affinities to the target protein and key molecular interactions within the EGFR tyrosine kinase domain. The compounds identified and evaluated through this computational approach represent promising candidates for further structural optimization and *in vitro* experimental validation.

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Sciforum-211025: Sulfonamide- and Coumarin-Tethered Acylhydrazones: Synthesis and Human Carbonic Anhydrases Inhibitory Activity

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Carbonic anhydrases (CAs) are zinc metalloenzymes catalyzing the reversible hydration of CO_2. Among the 15 human isoforms, hCA IX and hCA XII are transmembrane, tumor-associated enzymes overexpressed under hypoxic conditions. These isoforms promote extracellular acidification in the tumor microenvironment, facilitating cell survival, invasion, and metastasis, and have thus been validated as antitumor drug targets[1]. However, achieving selectivity for these isoforms over the cytosolic hCA I and hCA II remains a major challenge.

Sulfonamide derivatives constitute classical CA inhibitors (CAIs), with the deprotonated sulfonamide nitrogen coordinating the Zn^{+2} ion in the active site. Coumarins act as prodrug CAIs, with their hydrolysis products binding at the variable active-site entrance and conferring isoform selectivity toward hCA IX and hCA XII.[2]

Herein, we report the synthesis of two novel acylhydrazone families. The synthetic route began with the esterification of five aromatic carboxylic acids with methanol; followed by treatment of the resulting methyl esters with hydrazine hydrate to afford the corresponding acylhydrazides. Condensation of four aromatic acylhydrazides with coumarin-6-carboxaldehyde and five with 4-sulfamoylbenzaldehyde afforded nine novel acylhydrazones, which were characterized and evaluated for their inhibitory activity against hCA I, II, IX, and XII using a stopped-flow CO_2 hydration assay. All compounds showed potent inhibition of the four evaluated hCA isoforms, with Ki values in the micromolar to nanomolar range, whereas the coumarin-derived acylhydrazones displayed pronounced selectivity for the tumor-associated CA IX ($>$1000) and XII ($>$1300).

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Author contributions: Investigation, Martin Josue Torres Castaño and Macarena Soledad Le Pors; Writing - original draft, Martin Josue Torres Castaño; Writing - review and editing, Pedro Alfonso Colinas; Supervision, Macarena Soledad Le Pors and Pedro Alfonso Colinas; Funding acquisition, Pedro Alfonso Colinas;



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Sciforum-211030: Computational Multi-Target Profiling of Euphorbia Metabolites as Promising Anti-Cancer Candidates

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Background. According to the World Health Organization, cancer affects millions of individuals worldwide and imposes substantial physical, emotional, and financial burdens, claiming more than 26,000 lives each day. Cancer comprises a heterogeneous group of diseases that can arise in virtually any tissue.

Aim. Identifying metabolites derived from Euphorbia as potential therapeutic candidates for cancer treatment through in silico molecular docking.

Method. Euphorbia metabolites(44) were searched for (PubMed, ScienceDirect, Scopus), and their SMILES strings were obtained from PubChem or generated using ChemSketch. Nineteen cancer-related proteins from the PDB were selected and visualised in PyMOL. Multi-target docking was performed using AutoDock Vina 1.2.5 (boxes defined in AutoDockTools 1.5.7), and the results were analysed in PyMOL and Discovery Studio.

Results. In general, the molecules bind favourably to various receptors; however, certain structures display comparatively higher affinity for specific targets. Based on these patterns, three molecules were selected for further analysis: Zagrosin II (molecule 25), esculetin (molecule 15), and euphorbentin (molecule 16). Zagrosin II, a spirocyclic terpenoid, shows preferential binding to AKT1 and several nuclear receptors, including progesterone, oestrogen, and androgen receptors. Esculetin interacts with the aryl hydrocarbon receptor and PARP-1, and also with nuclear receptors—although to a lesser extent than Zagrosin II—through distinct biochemical pathways. Owing to its catechol moiety, esculetin may additionally participate in reactive oxygen species generation. Euphorbentin, structurally related to esculetin but containing two catechol rings, targets PARP-1 at the DNA level, AKT1 within signalling pathways, and COX-2 in inflammatory processes.

Conclusions. Species of the genus *Euphorbia* contain diverse metabolites that exhibit meaningful interactions with multiple cancer-related molecular targets. Among them, Zagrosin II emerges as the most promising candidate, given its dual activity on the AKT1 signalling pathway and hormone receptors, suggesting potential applicability in hormone-receptor-positive breast cancer.

Author contributions: Conceptualization, Christian Ruben HualtibambaGonzales and Víctor Eduardo Villarreal La Torre; Methodology, Christian Ruben HualtibambaGonzales and Víctor Eduardo Villarreal La Torre; Software, Christian Ruben HualtibambaGonzales and Víctor Eduardo Villarreal La Torre; Validation, Christian Ruben HualtibambaGonzales and Víctor Eduardo Villarreal La Torre; Formal analysis, Christian Ruben HualtibambaGonzales and Víctor Eduardo Villarreal La Torre; Investigation, Christian Ruben HualtibambaGonzales and Víctor Eduardo Villarreal La Torre; Resources, Víctor Eduardo Villarreal La Torre; Data curation, Víctor Eduardo Villarreal La Torre; Writing - original draft, Christian Ruben HualtibambaGonzales; Writing - review and editing, Víctor Eduardo Villarreal La Torre; Visualization, Christian Ruben HualtibambaGonzales; Supervision, Víctor Eduardo Villarreal La Torre;



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Sciforum-211086: Aloin and Its Metabolite Modulate Prognosis and Immune Microenvironment in Head and Neck Squamous Cell Carcinoma via Gut Microbiota Metabolite-Related Targets

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Aloin modulates the composition and function of the gut microbiota, and gut microbiota can also convert aloin to aloe-emodin, which may further contribute to its biological effects. Additionally, gut microbiota-derived metabolites are known to shape the immune microenvironment of head and neck squamous cell carcinoma (HNSCC) via the “gut-immune axis.” However, whether aloin and its metabolite affect HNSCC prognosis and immune landscape via gut microbiota metabolite-related gene targets remains unclear. In this study, aloin-related targets were retrieved from SwissTargetPrediction, CTD, and PharmMapper, and gut microbiota metabolite-regulated genes were obtained from gutMGene. Using the TCGA-HNSCC cohort, a risk score signature was constructed through univariate Cox, LASSO, and multivariate Cox, and its independent prognostic value was evaluated after adjusting for clinical covariates. Associations between risk score and immune cell infiltrates were assessed, along with KEGG enrichment and molecular docking. Intersection yielded 29 common targets, from which six hub genes were identified to build a risk score signature: Risk score = (-0.1324)×BCL2 + (0.2392)×PPARG + (0.1031)×NQO1 + (0.2453)×APP + (-0.0657)×LYZ + (0.0367)×EGFR. Multivariate Cox confirmed the risk score as an independent prognostic factor for HNSCC ($P < 0.05$). Immune infiltration analysis showed that the risk score positively correlated with $CD4^+$ T cells, central memory T cells, follicular helper T cells, and macrophages, and negatively with effector memory T cells and neutrophils ($P < 0.05$). KEGG enrichment revealed significant enrichment in HIF-1, JAK-STAT, PPAR and PD-L1/PD-1 checkpoint pathways. Molecular docking revealed that aloin and aloe-emodin bound to PPARG (PDB: 8B95; -8.4/-8.6 kcal/mol) and APP (PDB: 2FK1; -5.3/ -5.2 kcal/mol), supporting their multi-target potential. Collectively, aloin and its metabolite may influence HNSCC prognosis and immune microenvironment potentially through the gut-immune axis, offering a theoretical basis for prognostic assessment and aloin-based therapeutic strategies.

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Sciforum-211096: Design, Synthesis, Biological Evaluation, and Computational Investigation of 2,7-Dimethylimidazo[1,2-a]pyridine-3-carboxamide Derivatives as Novel α-Amylase Inhibitors

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A series of substituted 2,7-dimethylimidazo[1,2-a]pyridine-3-carboxamide derivatives (Va–Vm) was synthesized and evaluated for their α-amylase inhibitory activity as potential antidiabetic agents. In vitro screening identified Vg, Vd, and Vk as the most active derivatives, with IC_{50} values of 197.5, 204.4, and 207.6 µg/mL, respectively, compared with 66.65 µg/mL for the reference inhibitor acarbose. Molecular docking studies against α-amylase revealed favorable binding affinities for the synthesized derivatives, ranging from -7.4 to -8.7 kcal/mol. Among the tested compounds, Vg exhibited the most favorable binding profile, engaging key catalytic and binding-site residues through hydrophobic, hydrogen-bonding, π–π stacking, halogen-bonding, and π–cation interactions. The stability of the Vg–α-amylase complex was further investigated by 100 ns molecular dynamics simulations, which demonstrated sustained ligand binding, limited structural fluctuations, and stable protein–ligand interactions throughout the simulation. MM/GBSA calculations further supported the favorable binding free energy of the lead compounds. In silico ADME profiling predicted favorable pharmacokinetic characteristics, including high gastrointestinal absorption, low topological polar surface area, blood–brain barrier permeability, and compliance with Lipinski's rule of five. Furthermore, toxicity prediction indicated no major safety liabilities. Overall, the integrated experimental and computational results identify substituted 2,7-dimethylimidazo[1,2-a]pyridine-3-carboxamides, particularly Vg, as promising lead structures for further optimization and development as α-amylase inhibitors for potential application in diabetes management.

Author contributions: Conceptualization, Suraj N. Mali; Methodology, Suraj N. Mali and Rakesh Somani; Software, Suraj N. Mali and Rakesh Somani; Validation, Rakesh Somani; Writing - original draft, Suraj N. Mali and Akash Sanjay Pandey; Writing - review and editing, Suraj N. Mali and Akash Sanjay Pandey; Supervision, Rakesh Somani;



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Sciforum-211156: Development of Novel Enantiopure Aminopyridine Alcohols as Promising Antimalarial Agents

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Malaria remains a major global public health challenge, particularly in sub-Saharan Africa. According to the World Health Organization, malaria cases increased by 3% compared with 2023, reaching 282 million cases with approximately 610,000 deaths in 2024. The disease is caused by *Plasmodium* parasites, transmitted through the bites of female *Anopheles* mosquitoes. Among the five *Plasmodium* species infecting humans, *P. falciparum* is the most prevalent species in Africa and the most lethal. The emergence and spread of resistance to artemisinin-based combination therapies (ACTs), the first-line treatments recommended by the WHO, represent a major threat to malaria control.

Resistance to ACTs has been associated with mutations in the *pf*k13 gene, which are linked to artemisinin resistance, as well as alterations in *Pf* multidrug resistance 1 (*Pf*MDR1), a transporter involved in the influx of nutrients and molecules, including arylaminoalcohols from the parasite cytosol into the digestive vacuole. These genetic and molecular adaptations compromise the efficacy of ACTs, highlighting the critical need for the development of new antimalarial agents.

Herein, we report the design and synthesis of 30 novel enantiopure aminopyridine alcohols based on both the enpiroline scaffold and a first hit identified by our team. A short and optimized synthetic route was developed, and the resulting compounds were evaluated for their physicochemical properties and *in vitro* antiplasmodial activity. Most compounds exhibited strong antiplasmodial activity against both the 3D7 and W2 *P. falciparum* strains, with IC_{50} values below 50 nM. Cytotoxicity assays against a mammalian cell line revealed excellent selectivity indices, mostly exceeding 150. Structure-activity relationship studies identified key substituents that enhanced antimalarial activity and selectivity, highlighting a promising compound. Further studies will focus on characterizing its pharmacokinetic properties and evaluation of its *in vivo* efficacy to confirm whether this promising compound can be validated as a new antimalarial hit.



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Sciforum-211265: ABTS $^{\bullet+}$ Radical Quenching by Copper(II) Complexes of Salicylaldehyde Thiosemicarbazoneswith Streptocide

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The development of new antioxidant compounds is of considerable interest because excessiveproduction of reactive oxygen species can disrupt cellular redox homeostasis and contribute tovarious diseases. Thiosemicarbazones and their transition metal complexes have emerged aspromising biologically active systems, exhibiting antioxidant, antimicrobial, and anticancerproperties. In particular, copper(II) complexes of thiosemicarbazone derivatives havedemonstrated diverse biological activities [1], while the incorporation of sulfonamide fragments mayprovide an additional opportunity to modulate the biological properties of these compounds.The aim of this study was to synthesize copper(II) complexes with salicylaldehyde 3-methoxyphenylthiosemicarbazone (H_2L^1) and 4-methoxyphenylthiosemicarbazone (H_2L^2) andstreptocide, and to investigate their antioxidant activity against the ABTS$^{\bullet+}$ cation radical.The copper(II) complexes were obtained by reaction between copper(II) acetate monohydrate,the corresponding thiosemicarbazone, and streptocide in a 1:1:1 molar ratio in ethanol. Theobtained compounds, Cu(Str)L^1 and Cu(Str)L^2, were characterized by FTIR spectroscopy,elemental analysis, and molar conductivity measurements to confirm their composition andstructural features.The antioxidant activity of the synthesized complexes, as well as their starting materials, wasevaluated against the ABTS$^{\bullet+}$ cation radical. All starting compounds were inactive, whereas thesynthesized copper(II) complexes demonstrated pronounced antioxidant activity, with values of27.02 μM for Cu(Str)L^1 and 22.21 μM for Cu(Str)L^2. Trolox, a widely used referenceantioxidant, was employed as a standard for comparison. Both synthesized complexes exhibitedhigher antioxidant activity than Trolox, demonstrating the beneficial effect of copper(II)coordination and the incorporation of the streptocide fragment on the antioxidant properties ofthe resulting compounds.This work was fulfilled with the financial support of the subprograms 010602 and 010701 of theinstitutional project.

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Sciforum-211297: Pyruvic Acid 4-Allylthiosemicarbazone and Its Metal Complexes as Agents for Free Radical Neutralization

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The search for novel biologically active compounds capable of scavenging reactive radical species is of considerable interest due to the involvement of oxidative stress in numerous pathological processes. Pyruvic acid, a naturally occurring metabolite, represents a promising structural fragment for the design of biologically active compounds. Thiosemicarbazones are also well known for their diverse pharmacological properties, including antiradical activity. Thus, the combination of pyruvic acid fragment with the thiosemicarbazone moiety may represent a promising strategy for the development of new potential radical-scavenging agents. The aim of this work was to synthesize pyruvic acid 4-allylthiosemicarbazone (H_2L) and its metal complexes, and to investigate their antiradical activity against the $ABTS^{\bullet+}$ cation radical.

For this purpose, the ligand was first synthesized by the reaction between pyruvic acid and 4-allylthiosemicarbazide in a 1:1 molar ratio in ethanol. To obtain the metal complexes $[Cu(HL)NO_3]$, $[Ni(HL)_2]$ and $[Fe(HL)_2]NO_3$, copper(II), nickel(II), and iron(III) salts reacted with the 4-allylthiosemicarbazone in 1:1 and 1:2 molar ratios in hot ethanol. The obtained compounds were characterized using FTIR spectroscopy, elemental analysis, molar conductivity measurements, and single-crystal X-ray diffraction analysis.

The antiradical activity for all synthesized compounds was evaluated against the $ABTS^{\bullet+}$ cation radical. The results showed that the copper(II) complex did not exhibit antiradical activity. In contrast, coordination of the ligand to nickel(II) and iron(III) ions resulted in enhanced antiradical activity of the corresponding complexes with activity values of 4.11 μM and 14.80 μM, respectively. The antiradical activity of these compounds was found to be 2 - 8 times higher than that of Trolox, used as a reference antioxidant.

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Sciforum-211312: Design, Synthesis, and Biological Evaluation of Novel Anthranilate Derivatives as Potential NLRP3 Inhibitors

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AimChronic inflammation contributes to tumor initiation and progression, with the NLRP3 inflammasome promoting IL-1β–mediated signaling, angiogenesis, and immune evasion. Tranilast, an anthranilate derivative, directly inhibits NLRP3 oligomerization and serves as a promising scaffold for next-generation inhibitors. This study aims to design and synthesize novel Tranilast-based anthranilate derivatives with improved predicted binding to the inactive conformation of NLRP3.

Methods

A structure-based drug design approach guided scaffold modifications, with preliminary molecular docking used to prioritize promising substitution patterns. The designed derivatives were synthesized through a multistep pathway centered on an anthranilate scaffold, incorporating sulfonamide introduction and subsequent structural refinements. The synthesized compounds were purified and characterized using melting point determination, thin-layer chromatography, infrared spectroscopy, and nuclear magnetic resonance and mass spectrometric analysis.

Key Findings

The synthetic workflow successfully produced a diverse series of anthranilate-based derivatives through sulfonamide formation and further scaffold modifications. Each step proceeded efficiently under optimized conditions, yielding structurally clean intermediates and final compounds verified by spectroscopy. Preliminary docking supported the design rationale by predicting favorable interactions with inactive NLRP3. The resulting compound library demonstrates the practicality of the synthetic strategy and provides tranilast-based derivatives ready for subsequent biological evaluation.

ConclusionThis study establishes a rational workflow integrating scaffold redesign, docking-based prioritization, and synthetic chemistry to generate new anthranilate derivatives with improved predicted affinity for NLRP3. The synthesized and characterized compounds will be subjected to future biological screening to evaluate their ability to modulate NLRP3-mediated inflammatory responses and to determine their potential as anticancer and anti-inflammatory candidates.

Author contributions: Supervision, Ahmed Thabet Negmeldin and Eman Moussa El-labbad;



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Sciforum-211375: Investigation of the mechanism of action of a selective inhibitor of the main protease of beta-coronaviruses using the recombinant 3CLpro protein

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As a result of in vitro screening, a number of 3CLpro inhibitors were identified as an N-acylated dipeptide with the C-terminal aldehyde group (“warhead”), which forms a thioacetal covalent bond with cysteine residue 145 (Cys145) in the enzyme’s active site to block protease function. This mechanism is quite reliable and applied in the design of various serine proteases inhibitors. IC50 of the lead compound—N-(4-methyl-1-oxo-1- ((1-oxo-3-(2-oxopyrrolidin-3-yl)propan-2-yl)amino)pentan-2-yl)-[1,1'-biphenyl]-4-carboxamide (Ph-Ph-Leu-oxPyr-CHO) was 5.8 mM. A test system for screening inhibitors of the main SARS-CoV-2 protease (3CLpro), based on the use of recombinant 3CLpro expressed in Escherichia coli and the visualization of substrate cleavage results via electrophoresis was used to investigate the mechanism of action of the lead compound Ph-Ph-Leu-oxPyr-CHO. The proposed method provided a reliable platform for studying the direct inactivating effect on 3CLpro. Experiments were conducted using twofold dilutions of the inhibitor Ph-Ph-Leu-oxPyr-CHO in 50 mM Na_2HPO_4/KH_2PO_4 buffer (pH 5.2) at 37°C for 20 hours. The results of the comparison between the Ph-Ph-Leu-oxPyr-CHO and Nirmatrelvir inhibitors suggest that the inhibitors have similar inhibitory activity, making Ph-Ph-Leu-oxPyr-CHO a promising candidate for further research. As a negative control, similar experiment was conducted using only the inhibitor solvent dimethyl sulfoxide (DMSO); no inhibition of 3CLpro enzymatic activity was observed, confirming the accuracy of the assay system and the significant effect of the inhibitors on the 3CLpro cleavage profile in the previous experiments.

Author contributions: Conceptualization, Timur Garaev; Methodology, Timur Garaev and Alexei Prilipov; Software, Timur Garaev; Validation, Maria Sergeevtseva and Alexei Prilipov; Formal analysis, Maria Sergeevtseva and Alexei Prilipov; Investigation, Maria Sergeevtseva; Data curation, Alexei Prilipov; Writing - original draft, Timur Garaev; Writing - review and editing, Timur Garaev; Supervision, Timur Garaev and Tatiana Grebennikova; Project administration, Tatiana Grebennikova;



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Sciforum-211422: 2-Formylpyridine 4-Allylthiosemicarbazone Copper(II) Complexes: Enhanced Anticancer Activity against THP-1 Cells

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Despite significant advances in cancer therapy, the development of novel selective anticancer agents remains an important research priority. Among various classes of bioactive compounds, thiosemicarbazones have attracted considerable attention because of their structural versatility and promising antiproliferative activity against different cancer cell lines. In this context, the THP-1 human monocytic leukemia cell line represents a relevant model for investigating the anticancer potential of newly developed thiosemicarbazone derivatives and their metal complexes. The aim of this study was to synthesize 2-formylpyridine 4-allylthiosemicarbazone (HL) and its copper(II) complexes and to investigate their anticancer activity against the THP-1 human monocytic leukemia cell line.

For this purpose, the HL was synthesized by the reaction between 4-allylthiosemicarbazide with 2-formylpyridine in ethanol. To obtain the copper(II) complexes $[Cu(L)(Cl_2CHCOO)]_2$ and $[Cu(L)(NO_3)]_2$, the ligand reacted with copper(II) dichloroacetate monohydrate and copper(II) nitrate trihydrate in a 1:1 molar ratio in ethanol. All obtained compounds were characterized using modern physicochemical analysis techniques.

The anticancer activity of these compounds against the human acute monocytic leukemia THP-1 cell line was evaluated using the MTS assay. The ligand demonstrated good activity, with an IC_{50} value 0.11 μM, while its coordination to the copper(II) ion resulted in a significant enhancement of the activity of the corresponding complexes by 15 - 17-fold.

Overall, the obtained results demonstrate that coordination of the 2-formylpyridine 4-allylthiosemicarbazone ligand with copper(II) significantly enhances its anticancer activity against THP-1 cells, highlighting copper complexes as promising candidates for further investigation as potential anticancer agents.

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Sciforum-211464: New Profen-Derived Methoxyaryl Ketones: Synthesis and Structural Characterization

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This study reports the design and synthesis of novel profen-derived hybrid compounds incorporating methoxyaryl fragments. The approach combines the well-established anti-inflammatory pharmacophores of profen-class NSAIDs with the structural and pharmacological versatility of methoxylated aromatic systems. The target ketone-based hybrids were efficiently synthesized through Friedel–Crafts acylation using polyphosphoric acid (PPA) as an efficient, reusable, and solvent-minimized acidic medium, enabling regioselective coupling under mild reaction conditions. Systematic optimization of the reaction parameters resulted in high conversion while minimizing the formation of undesired by-products.

A total of ten novel hybrid compounds were synthesized. Five compounds were obtained by acylation of ibuprofen, ketoprofen, naproxen, flurbiprofen, and carprofen with anisole, while five structurally related derivatives were prepared using veratrole as the methoxyaryl coupling partner. The structures of all newly synthesized compounds were confirmed by comprehensive spectroscopic and analytical characterization, including proton and carbon 13 NMR spectroscopies, infrared (IR) spectroscopy, and high-resolution mass spectrometry (HRMS).

The incorporation of electron-donating methoxyaryl groups into profen-derived scaffolds provides additional structural diversity and may facilitate favorable interactions within biological binding sites. The resulting hybrid ketones represent promising molecular frameworks for further pharmacological investigation. Overall, this study demonstrates the potential of a sustainable, solvent-minimized Friedel–Crafts acylation strategy for the development of structurally diverse profen-based hybrids and provides new scaffolds for future studies addressing inflammatory and other pharmacologically relevant targets.

Author contributions: Conceptualization, Stanimir Manolov; Methodology, Stanimir Manolov; Software, Dimitar Georgiev Bojilov; Validation, Dimitar Georgiev Bojilov; Formal analysis, Diyana Dimitrova; Investigation, Diyana Dimitrova and Iliyan Ivanov; Resources, Iliyan Ivanov; Data curation, Dimitar Georgiev Bojilov; Writing - original draft, Stanimir Manolov; Supervision, Stanimir Manolov and Iliyan Ivanov; Project administration, Stanimir Manolov;



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Sciforum-211476: Synthesis-Driven In Silico Exploration of Functionalized Indolin-2-One Heterodimers: Reverse Docking, ADMET, and Antibacterial Evaluation

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The discovery of multifunctional small molecules addressing interconnected biological pathways represents an urgent challenge in modern medicinal chemistry and drug design. In this work, we report the rational exploration and multifaceted in silico profiling of novel functionalized heterocyclic heterodimers as prospective bioactive candidates. Initial structural optimization in the MM2 force field was coupled with proteome-wide blind reverse docking via the GalaxySagittarius protocol (GalaxyWeb platform) to identify putative pharmacological targets without prior bias. The screened compounds exhibited pronounced multitarget affinity profiles (binding free energies reaching -27.4 kcal/mol) across several clinically validated disease-modifying axes: immune checkpoint modulation (Siglec-7, ΔG = -27.4...-26.2 kcal/mol), lipid homeostasis and metabolic regulation (PPARγ and FABP4), oncogenic protein kinases governing cell cycle and neoangiogenesis (VEGFR2, CDK6, p38α/MAPK14, and c-Abl, ΔG up to -26.1 kcal/mol), and epigenetic transcriptional readers (BET family bromodomains BRD2 and BRD4). Focused molecular docking utilizing AutoDock Vina was additionally engaged to refine specific ligand–receptor binding conformations and binding energies at the active sites. The pharmacokinetic profile, gastrointestinal absorption, membrane permeability, and safety endpoints were evaluated through in silico ADMET prediction, highlighting favorable drug-likeness and absence of critical liability alerts. Furthermore, computational assessment of antibacterial potential indicated promising broad-spectrum antibacterial capability. Together, these preliminary findings validate this novel hybrid architecture as a versatile small-molecule platform with high translational value for oncology, metabolic disorders, and infectious disease therapies.

Author contributions: Conceptualization, Vladislava Shramenko, Alexander V. Bespalov and Victor V. Dotsenko; Methodology, Vladislava Shramenko, Alexander V. Bespalov and Victor V. Dotsenko; Software, Alexander V. Bespalov and Victor V. Dotsenko; Investigation, Vladislava Shramenko; Resources, Victor V. Dotsenko; Writing - original draft, Vladislava Shramenko; Visualization, Vladislava Shramenko; Project administration, Vladislava Shramenko; Funding acquisition, Victor V. Dotsenko;



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Sciforum-211505: Mechanosynthesis and Biological Evaluation of Valproic Acid–Based Dual-Pharmacophore Hybrids

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This study reports the green mechanosynthesis of nine novel hybrid molecules combining valproic acid-a clinically established anticonvulsant, mood stabilizer, and epigenetic modulator-with bioactive 2-phenylethylamine and tryptamine derivatives, which are recognized for their neuromodulatory, antioxidant, and anti-inflammatory properties. The hybrids were efficiently prepared by initially converting valproic acid to its corresponding acid chloride, followed by rapid, solvent-minimized amidation with various substituted amines under optimized planetary ball-milling conditions (500 rpm, 1 minute). This eco-friendly protocol achieved excellent yields (> 90%) while drastically reducing chemical waste and energy consumption.

All newly synthesized amide-linked compounds were rigorously characterized using ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectroscopy, infrared (IR) spectroscopy, and high-resolution mass spectrometry (HRMS). The strategic incorporation of a stable amide bond merges the neuroprotective potential of valproic acid with the radical-scavenging capabilities of the amine scaffolds. Subsequent in vitro evaluations, facilitated by a novel biodegradable deep eutectic solvent (urea and propylene glycol), demonstrated that these dual-pharmacophore hybrids exhibit potent hydrogen peroxide and hydroxyl radical-scavenging activities, alongside superior anti-inflammatory effects in albumin denaturation assays compared to standard references. Supported by favorable in silico molecular docking to human serum albumin, this work highlights how sustainable, solvent-minimized mechanochemistry can effectively accelerate the development of multifunctional, structurally optimized drug leads for neurological and inflammatory therapeutic research.

Author contributions: Methodology, Stanimir Manolov; Software, Dimitar Georgiev Bojilov; Formal analysis, Diyana Dimitrova; Investigation, Stanimir Manolov and Dimitar Georgiev Bojilov; Writing - original draft, Diyana Dimitrova and Iliyan Ivanov; Supervision, Iliyan Ivanov; Project administration, Stanimir Manolov; Funding acquisition, Iliyan Ivanov;



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Sciforum-211593: Synthesis and evaluation of anticancer activity of spiro-fused pyrrolo[3,4-c]pyrroles against tumor cell lines

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Oncological diseases remain a major global health challenge and one of the leading causes of mortality despite decades of research and improvements in multimodal treatment strategies including radiation, surgery, and chemotherapy. Therefore discovery of novel chemotherapeutic agents with improved efficacy and safety profiles as well as methods of their target delivery remains a critical objective in medicinal chemistry. Heterocyclic compounds, particularly spirocyclic pyrrolo[3,4-c]pyrrole derivatives, are privileged scaffolds in drug design.This study devoted to the development of synthetic methods and the study of the biological activity of new, first-synthesized classes of spirocyclic compounds, namely spiro-fused pyrrolo[3,4-c]pyrroles, pyrrolo[3,4-a]pyrrolizines, and pyrrolo[3′,4′:3,4]pyrrolo[1,2-c]thiazoles containing tetramethylcyclopentane and camphor moieties. These classes of compounds were obtained as a result of 1,3-dipolar cycloaddition reactions of differently substituted maleimides to azomethine ylides, which were first synthesized by condensing camphoroquinone and cyclopentanedione with various α-amino acids. These cycloadditions proceed smoothly under optimized reaction conditions to give corresponding products in moderate to good yields and moderate to high diastereoselectivity.The synthesized compounds were preliminary screened for their *in vitro* antiproliferative activity against the human erythroleukemia cell line K-562 by the standard MTS assay.The results revealed that several adducts exhibited significant cytotoxic effects, with half-maximal inhibitory concentration (IC_{50}) values as potent as 15 μg/mL. These findings substantiate the promising antitumor potential of the synthesized spirocyclic derivatives and warrant further investigation.



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Sciforum-211619: Benzylidene-9(10*H*)-anthracenones: Synthesis, SAR and Binding Mode of a novel CK2 Inhibitor Class

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The human protein kinase CK2 is a constitutively active and ubiquitously expressed serine/threonine kinase involved in numerous cellular processes, including cell survival and proliferation, cell cycle progression and regulation of apoptosis. These functions are primarily mediated through phosphorylation of hundreds of substrates, thereby modulating key signaling pathways. Structurally, CK2 is a tetramer, which consists of two catalytic (a or a') and two regulatory (ß) subunits. In several cancer cells, where CK2 is overexpressed, the phosphorylation of CK2 substrates promotes tumorigenesis and inhibits apoptosis. Consequently, inhibition of CK2 represents a promising strategy for cancer therapy. [1]

To expand our in-house library, we designed and synthesized a series of benzylidene-analogs derived from 9(10*H*)-anthracenone. Using a CE-based CK2 assay, we identified several compounds with nanomolar inhibitory potency against the CK2 holoenzyme. [2] SAR analysis revealed that the inhibitory potency is strongly dependent on the substitution pattern of the terminal phenyl ring, which therefore became the focus of further structural optimization.

Co-crystallization with CK2a' confirmed that the planar and hydrophobic anthracenone scaffold occupies the ATP/GTP binding site of CK2. This finding is consistent with previous structural data [3] and rationalizes the observed potencies.

Herein, we report the synthesis and preliminary biochemical data of a series of benzylidene-9(10*H*)-anthracenones, with the most potent analogs displaying IC_{50} values below 20 nM. Our data shows 9(10*H*)-anthracenone derived inhibitors as promising candidates for the development of potent CK2 inhibitors.

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Sciforum-211781: Optimization of the conditions for the nucleophilic aromatic substitution reaction of 2,4,5-trichloropyrimidine

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2,4,5-Trichloropyrimidine is an important reagent for the synthesis of various tyrosine kinase inhibitors; however, its reactivity decreases significantly with each substituted chlorine atom. Thus, the substitution of the second chlorine atom located in the fourth position is the limiting step in the synthesis of the target compounds.

Currently, there are two main methods for replacing the second chlorine atom: 1) heating in alcohol without adding additional reagents, 2) heating in DMF with the use of palladium catalysts.

To optimize the first method, reagents were used to create either basic or acidic conditions. Thus, carrying out the reaction in IPA without using additives did not yield a positive result; adding K_2CO_3 or Et_3N also did not lead to the formation of the target product, while adding HCl resulted in the production of product without Boc with a yield of 7 %.

According to the second method, no product is formed in the absence of a catalyst, but when $Pd(OAc)_2$ was added, a reaction yield of 24 % was achieved. Other palladium catalysts will be considered for further optimization.

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Sciforum-211862: Evaluating the cell cycle modulation activity of synthetic halogenated chalcogens

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The adverse effects of conventional cancer treatments are driving growing interest in new therapies. Derivatized chalcone emerges as promising anticancer solutions to this deadly disease. Aromatic acetophenone and halogenated benzaldehydes were used to synthesize chloro and bromo chalcone derivatives. The synthetic chalcone analogues have been characterized by IR and NMR spectroscopy. The cytotoxicity of halogenated chalcone and the cell cycle analysis were carried out by means of MTT and flow cytometry respectively on MCF-7 and HCT-116 cell lines. The synthesized analogs showed cytotoxicity in selected cancer cell lines. The halogenated chalcogens were found better than the standard chalcone. Analysis of the cell cycle reveals the relative proportion of cells in the various stages of the cell cycle. Synthesized halogenated chalcone analogues show reduced cell viability at the G2 and S phases of the cell cycle.

Author contributions: Conceptualization, Surendra Prakash Gupta; Methodology, Akanksha Shrivastava; Validation, Surendra Prakash Gupta; Formal analysis, Akanksha Shrivastava and Surendra Prakash Gupta; Investigation, Akanksha Shrivastava; Writing - original draft, Akanksha Shrivastava; Writing - review and editing, Surendra Prakash Gupta; Supervision, Surendra Prakash Gupta;



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Sciforum-211897: Developing Novel Molecules to Prevent Amyloid-Beta Aggregation

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Alzheimer's Disease (AD) affects and estimated 700,000 Canadians, a figure projected to grow to 1.7 million by 2050. Current treatment options are limited and there is no cure for the disease. One of the prevailing explanations for the cause of AD is the amyloid hypothesis, which posits that aggregates of amyloid-beta (Aβ) are the initiating pathological agents. Aβ self-assembles in the brain of AD patients, and these aggregates cause neuronal damage through several routes, including oxidative stress, membrane dysfunction, and causing synaptic dysfunction. Small molecules capable of inhibiting or modulating the formation of Aβ aggregates are therefore valuable both as potential therapeutics and as tools for understanding disease progression.

This project involves designing and evaluating novel phenylacetylene derivatives as inhibitors of Aβ aggregation. A novel compound library was designed using molecular docking with Aβ aggregate models, then synthesized using a two-step procedure: a Sonogashira coupling between an aryl bromide and trimethylsilylacetylene, followed by a base-catalyzed deprotection. Products were then characterized using ^{1}H NMR, ^{13}C NMR, and LCMS to confirm purity.

The ability of these phenylacetylenes to prevent Aβ aggregation was assessed using a fluorescence-based kinetics assay. Aggregate morphology in the presence of promising inhibitors was assessed using transmission electron microscopy (TEM). The safety profile of the phenylacetylenes was tested in mouse hippocampal (HT 22) neuronal cells. Future work will further test their ability to rescue neuronal cells from Aβ-mediated cytotoxicity.

The data collected in this project will be used to develop a structure activity relationship (SAR) for phenylacetylenes to determine their potency in inhibiting Aβ aggregation. This work will contribute to both the development of potent small-molecule Aβ aggregation inhibitors, and to help understand the role Aβ aggregates play in Alzheimer's disease.



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Sciforum-213051: Design, Microwave-Assisted Synthesis and Druglikeness Evaluation of Two Chloroquine-Based Hybrids for Improved Resistance Profiles Against Malaria

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Malaria primarily affects children and pregnant women due to pregnancy-related immune suppression. Chloroquine-based chemotherapy, if potent, could be an ideal solution given chloroquine's pharmacokinetics that allow placental penetration in Pregnancy Associated Malaria (PAM) for example. Here, we report the design, synthesis and druglikeness evaluation of chloroquine hybrids, CQF1 and CQF64 as potential dual-acting antiplasmodial agents with improved resistance profiles. Docking studies were done on *MOE v2019.01* against plasmepsin II (PDB: 1LEE) and *Pf*80s (PDB:5UMD). Chloroquine freebase from diphosphate was combined with triethylamine and tryptamine or 2-(chlorocarbonyl)phenyl acetate at 0^0C, microwave irradiated for 40 and 100 seconds respectively, and crude products triturated. Elucidation was by NMR, PDA-LC/MS, FTIR, etc. Molecular descriptors/predictions were from *SwissADME*, *ADMETlab_3.0* and *ToxAlerts* webservers. CQF64 showed a H-bonding interaction with Ser37 of Pl_II, and two pi-H interactions with Lys52 and Try53 of *Pf*80s. S-scores*_(Pl_II)* = -8.4333 & -7.8324 kcal/mol and S-scores*_(80s)* = -7.4578 & -7.0080 kcal/mol for CQF1 and CQF64 respectively. From these, predictive lipophilic ligand efficiency *(pLLE)* scores of 1.87 & 1.91 were computed. With the goal being to achieve balance between dual-functionality and druglikeness, these values are decent for hybrids. Spectral data were consistent with expected structures of the indole-based CQF1 (60.3% yield) and phenylacetate-based CQF64 (40.3%). Both were Ro5-compliant with 1 violation (cLogP) each. Quantitative Estimation of Druglikeness (QED) outrightly assessed CQF1 (0.411) as better than CQF64 (0.263), perhaps due to structural alerts. However, CQF64 having a lower lipophilicity (XLogP3 = 5.51) compared to CQF1 (6.07), lower melting point (67-72 vs 128-132^{0}C), and lower estimated aqueous solubility (LogS = -5.86 vs -6.05), may be considered more viable. Pending biological validation and optimisation, our findings suggest that CQF64 could give a useful dual-acting antiplasmodial agent.

Author contributions: Conceptualization, Joseph Chukwuebuka Oguegbulu; Methodology, Joseph Chukwuebuka Oguegbulu; Formal analysis, Joseph Chukwuebuka Oguegbulu; Investigation, Joseph Chukwuebuka Oguegbulu; Resources, Patrick M. Woster; Data curation, Joseph Chukwuebuka Oguegbulu; Writing - original draft, Joseph Chukwuebuka Oguegbulu; Writing - review and editing, Joseph Chukwuebuka Oguegbulu; Visualization, Joseph Chukwuebuka Oguegbulu; Supervision, Patrick M. Woster; Project administration, Patrick M. Woster;



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Sciforum-214408: Quinazoline Derivatives of Imino-1,2,3-dithiazoles as *Pseudomonas aeruginosa* Biofilm Dispersal Agents

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Biofilms represent a major clinical challenge, as bacteria embedded within these structures are highly tolerant of antibiotics. Among biofilm-forming pathogens, *Pseudomonas aeruginosa* is particularly problematic, as it forms persistent biofilms that cause acute and chronic infections, especially in immunocompromised patients.(1) Since chronic infections associated with biofilms require extensive treatment, they increase the risk of antimicrobial resistance.(2) In this context, novel therapeutic strategies are emerging, aiming to promote biofilm dispersion and thereby restore bacterial susceptibility to antimicrobial agents.

In this study, a library of thirty-six *N*-arylimino-1,2,3-dithiazole derivatives was investigated for their capacity to promote the dispersion of *P. aeruginosa* biofilms using a crystal violet-based assay.(3) The most active candidates were further evaluated to determine their impact on bacterial growth, virulence, and cytotoxicity toward human cell lines. In addition, fluorescence anisotropy experiments were performed to explore potential effects on bacterial membrane properties and provide preliminary mechanistic insights.

This study reveals that quinazoline-containing imino-1,2,3-dithiazoles exhibit biofilm-dispersing activity at micromolar concentrations. Importantly, these molecules do not impact bacterial growth dynamics of *P. aeruginosa*, do not enhance virulence, and exhibit no detectable cytotoxicity toward eukaryotic cells.

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Session 4. Natural Products and Biopharmaceuticals

Sciforum-200799: Computational Evaluation of Natural Polyphenols from *Cistus creticus* as Multitarget Antioxidants: Docking, PASS Prediction, and Pharmacokinetic Study

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Oxidative stress plays a central role in the pathogenesis of numerous chronic diseases, prompting the search for effective natural antioxidants with multitarget mechanisms of action. In this study, bioactive polyphenolic compounds identified from Cistus creticus were investigated using an integrated in silico approach combining molecular docking, PASS prediction, and ADMET analysis. Molecular docking was performed against the Keap1 protein (PDB ID: 2FLU) and the p22phox (PDB ID: 7YXW), two key regulators of oxidative stress. The results demonstrated strong binding affinities for most flavonoids, particularly hesperidin, quercetin, rutin, and their derivatives, which formed stable hydrogen bond interactions with critical amino acid residues involved in protein function. PASS prediction further supported these findings, revealing high probabilities of antioxidant activity (Pa $>$ 0.7) for the majority of compounds, especially myricetin, rutin, and quercetin derivatives. ADMET profiling indicated favorable safety characteristics for all compounds, including the absence of mutagenicity and hepatotoxicity, although glycosylated flavonoids showed limited permeability and potential P-glycoprotein efflux. Overall, the results suggest that polyphenolic compounds derived from Cistus creticus exhibit promising antioxidant potential through a dual mechanism involving activation of the Nrf2 signaling pathway and inhibition of reactive oxygen species production via the NADPH oxidase. This study highlights the relevance of integrating computational approaches to identify and optimize natural compounds as potential therapeutic agents against oxidative stress-related disorders.



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Sciforum-209204: Antidiabetic properties of methanol extract of *Dacryodes klaineana* leaf in alloxan-induced diabetic rats

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Objective: This study examined the impact of *Dacryodes klaineana* leaf methanol extract on various metabolic markers in Wistar rats with diabetes induced by alloxan. **Study design**: For 21 days, groups 3 and 4 of diabetic rats were given oral doses of 200 and 400 mg/kg of *D. klaineana* leaf methanol extract and 5 mg/kg of glibenclamide (standard group 3). Standard techniques were used to perform biochemical, hematological, and phytochemical assays. **Results**: From day 7 to day 21, treatment with *D. klaineana* leaf extract significantly reduced blood glucose levels ($p < 0.05$), which was similar to the impact of the commonly used drug glibenclamide. Rats treated with different doses of *D.klaineana* leaf methanol extract showed a substantial ($p<0.05$) increase in SOD, GSH, PCV, Hb, and RBC levels when compared to the untreated group. Total protein, HbA1c, WBC, MDA, AST, ALT, total bilirubin, urea, and uric acid concentrations were significantly ($p<0.05$) lower in the groups treated with different dosages of *D. klaineana* leaf methanol extract than in the untreated group. **Conclusion**: The results lend credence to *D. klaineana* leaf's potential as a natural remedy for diabetes.

Author contributions: Conceptualization, Chinelo Nkwocha; Methodology, Nene Chiaka-Onyemeze; Software, Chinelo Nkwocha; Validation, Nene Chiaka-Onyemeze; Investigation, Chinelo Nkwocha; Data curation, Nene Chiaka-Onyemeze; Writing - original draft, Chinelo Nkwocha;



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Sciforum-209907: Effects of *Morus alba* L. and *Morus nigra* L. Extracts on Memory Performance in a Scopolamine-induced Zebrafish Model

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Introduction: Cognitive decline observed in Alzheimer's disease is associated with cholinergic dysfunction and oxidative stress, making phytochemicals with combined antioxidant and anticholinesterase activity promising neuroprotective candidates. This study investigated the cognitive potential of hydroalcoholic *Morus alba* L. (MAE) and *Morus nigra* L. (MNE) leaf extracts in a scopolamine-induced zebrafish model.

Methods: MAE and MNE were phytochemically characterized by RP-UHPLC-PDA. The effects of MAE and MNE (1 and 10 µg/L) were evaluated against scopolamine (100 µM)-induced memory impairment in a zebrafish model (*Danio rerio*). Memory performance was assessed using the Y-maze and novel object recognition (NOR) paradigms, with galantamine (3.5 µM) serving as the reference compound. The antioxidant and anticholinesterase properties of the extracts were also assessed through hydroxyl radical scavenging and lipid peroxidation inhibition assays, to correlate the biochemical profile with the observed cognitive outcomes.

Results: RP-UHPLC-PDA profiling identified chlorogenic, caffeic and trans-ferulic acids, hyperoside and luteolin-7-glucoside among the most important compounds quantified in the extracts, with MNE exhibiting a higher overall polyphenol content. In the zebrafish model, scopolamine administration induced cognitive impairment, reflected by decreased exploratory preference in both the Y-maze and NOR tests. Treatment with *Morus* extracts improved memory performance, increasing responses to the novel arm in the Y-maze and preference for the novel object in the NOR test. MNE exhibited stronger antioxidant and cholinesterase-inhibitory activity than MAE.

Conclusions: These findings support MAE and MNE as multi-target neuroprotective candidates, combining behavioral efficacy with a favorable antioxidant and anticholinesterase profile.

Author contributions: Methodology, Maria Crina Isac;



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Sciforum-210062: Protective Effects of *Rosmarinus officinalis* and *Artemisia herba-alba* Against Glucose-Induced Oxidative Stress in Human Serum: An In Vitro Study

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Hyperglycemia is associated with impaired redox homeostasis and enhanced oxidative stress. This study aimed to evaluate the phytochemical composition and antioxidant activity of *Rosmarinus officinalis* and *Artemisia herba-alba* extracts and to investigate their protective effects against glucose-induced oxidative stress in human serum under *in vitro* conditions. Total polyphenol content (TPC) was determined using the Folin–Ciocalteu method, while total flavonoid content (TFC) was assessed using the aluminum chloride colorimetric method. Antioxidant activity was evaluated using the DPPH radical-scavenging assay. The protective effects of the extracts were further investigated in human serum samples exposed to increasing glucose concentrations (1, 10, and 100 mg/mL) by measuring total antioxidant status (TAS) and catalase (CAT) activity. Phytochemical analysis revealed that *Rosmarinus officinalis* showed a higher TPC than *Artemisia herba-alba* (81.87 ± 0.20 vs. 48.36 ± 5.19 mg GAE/g, respectively), whereas the TFC values were comparable between the two plants (26.32 ± 1.78 and 28.49 ± 0.15 mg QE/g, respectively). The ethanolic extract of *Artemisia herba-alba* exhibited strong DPPH radical-scavenging activity (IC_{50} = 0.71 mg/mL), while the aqueous extract of *Rosmarinus officinalis* also showed notable radical-scavenging activity (IC_{50} = 0.864 ± 0.36 mg/mL). Both extracts attenuated glucose-induced oxidative disturbances, as reflected by improvements in TAS and CAT activity in human serum samples. These findings indicate that *Rosmarinus officinalis* and *Artemisia herba-alba* possess antioxidant properties and may help mitigate glucose-induced oxidative disturbances in human serum.

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Sciforum-210378: Design and *in vitro* functional evaluation of M-6HIS-GLP-1-6HIS, a dual-hexahistidine-tagged GLP-1 variant

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Introduction: Native GLP-1 has a short half-life due to rapid enzymatic degradation, limiting therapeutic application. Sequence engineering may facilitate peptide production and purification but requires functional validation. We designed M-6HIS-GLP-1-6HIS, a recombinant GLP-1(7–37) variant carrying *N*- and *C*-terminal hexahistidine tags for affinity purification, and evaluated it in pancreatic β-cells.

Methods: M-6HIS-GLP- 1-6HIS was designed using sequence analysis. Structural modeling and analysis were performed with AlphaFold 3 and ChimeraX. A codon-optimized sequence was cloned into pET32(a), expressed in *E. coli* BL21(DE3) after 200 μM IPTG induction, and purified by Ni^{2+}-affinity chromatography. MIN6 cells served as a β-cell model. *Glp1r* expression was confirmed by qPCR. Cells were exposed to peptide (100 nM) for 24 h in glucose-free medium or medium containing 25 mM glucose. Metabolic activity, insulin secretion, and mitochondrial activity were assessed by MTT assay, ELISA, and fluorescence microscopy, respectively.

Results: Structural modeling predicted preservation of key peptide–GLP-1R contacts and an increased peptide–receptor interaction for M-6HIS-GLP-1-6HIS. In the MTT assay, cellular metabolic activity in peptide-treated MIN6 cells was 5.6% higher in the presence of 25 mM glucose than under glucose-free conditions. Insulin secretion increased in the presence of 25 mM glucose compared with glucose-free conditions ($p < 0.01$) and with the untreated control ($p < 0.05$). Mitochondrial fluorescence showed a distinct condition-dependent pattern. Under glucose-free conditions, M-6HIS-GLP-1-6HIS reduced relative MitoTracker fluorescence per cell compared with the untreated control ($p = 0.0044$). In peptide-treated cells, mitochondrial fluorescence increased in 25 mM glucose and was comparable to the untreated high-glucose control ($p = 0.79$).

Conclusions: M-6HIS-GLP-1-6HIS demonstrated a glucose-dependent insulin secretory response and glucose-associated changes in cellular metabolic and mitochondrial readouts in MIN6 cells. These findings support further functional investigation but do not establish GLP-1R-mediated agonism or DPP-4 resistance.

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Sciforum-210460: Korean mistletoe (*Viscum album* L. var. *coloratum* (Kom.) Ohwi) water extract inhibits viability and matrix invasion of MDA-MB-231 triple-negative breast cancer spheroids in three-dimensional culture

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Mistletoe (Viscum album L.) preparations are used clinically as complementary anticancer agents in Europe, yet most mechanistic work relies on lectin-enriched fractions and two-dimensional monolayer culture, which poorly reproduces drug penetration, hypoxic gradients and matrix-dependent invasion. Here we evaluated a crude water extract of Korean mistletoe (Viscum album L. var. coloratum (Kom.) Ohwi, syn. V. coloratum (Kom.) Nakai) in a three-dimensional spheroid model of MDA-MB-231 triple-negative breast cancer cells. The extract was prepared as described previously (Sci. Pharm. 2023;91:48) from dried mistletoe collected on oak trees in Gangwon-do, Korea (voucher VCA101), by threefold aqueous extraction at 4 °C and freeze-drying; it was not chemically characterised in this study. Spheroids were formed in basement-membrane extract and characterised from Day 0 to Day 7, compacting to 42.6 ± 0.4 % of Day 0 projected area by Day 1 and growing to 170.0 ± 4.5 % by Day 7. Viability after five days of treatment, measured by a water-soluble tetrazolium assay, fell dose-dependently from 96.8 ± 4.9 % at 78 µg/mL to 13.3 ± 5.6 % at 2500 µg/mL, giving a half-maximal inhibitory concentration of 504.6 ± 42.2 µg/mL and a twenty-percent inhibitory concentration of 237.5 ± 45.5 µg/mL by four-parameter logistic regression. Acridine orange/propidium iodide staining showed a concentration-dependent rise in propidium-iodide-positive signal. Invasion into basement-membrane extract, quantified as invaded area, did not differ between groups at Day 1 ($p > 0.6$). By Day 2 invaded area was reduced to 64.6 % and 48.2 % of the untreated control at the twenty-percent and half-maximal inhibitory concentrations respectively, and to 81.0 % and 72.1 % at Day 3; the two concentrations differed significantly at both time points. Korean mistletoe water extract therefore inhibits both viability and matrix invasion of triple-negative breast cancer spheroids, supporting further mechanistic study.



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Sciforum-210557: Molecular Docking Investigation of Glabridin Interaction with the VC1 Domain of RAGE

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Background: Receptor for advanced glycation end products (RAGE/AGER) is a multifunctional cell-surface receptor implicated in inflammatory and disease-associated signaling. Glabridin, a bioactive isoflavan isolated from licorice, has attracted interest because of its reported biological activities. However, its potential interaction with RAGE remains insufficiently characterized at the molecular level.

Objective: This study aimed to investigate the potential binding of glabridin to the VC1 domain of human RAGE using molecular docking and interaction analysis, with structural validation of the docking protocol.

Methods: The crystal structure of the RAGE VC1 domain (PDB ID: 6XQ3; Chain A; 1.71 Å) was used as the receptor. The crystallographic ligand V6Y was redocked using AutoDock Vina through PyRx for protocol validation. The redocked V6Y pose was compared with the experimental conformation using RMSD and protein–ligand interaction analysis. Glabridin was subsequently docked into the validated binding region. The top-ranked pose was analyzed using PLIP, and nine docking poses were compared to assess binding-region consistency.

Results: V6Y redocking reproduced the experimental binding orientation with an RMSD of 0.528 Å and a predicted affinity of -9.3 kcal/mol. Key π-cation interactions involving Lys52 and Lys110 were retained. Glabridin showed a best predicted affinity of -7.1 kcal/mol. The selected pose formed hydrogen bonds with Glu50 and Arg98, hydrophobic contacts with Ala21, Lys52, Arg98, Gln100, and Lys110, and a π-cation interaction with Arg98. Arg98 and Lys110 recurred across the nine poses despite differences in ligand orientation.

Conclusion: These findings support a potential glabridin–RAGE VC1 interaction and identify a recurrent binding region warranting further experimental investigation.



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Sciforum-210581: Exploring the Phytochemical and Anticancer Potential of Endophyte *Daldinia eschscholtzii* Isolated from *Clausena excavata*: An Integrated *In Vitro* and *In Silico* Approach

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Endophytic fungi maintain symbiotic relationships with plants and produce diverse secondary metabolites with significant therapeutic potential. This study aimed to characterize the phytochemicals and evaluate the anticancer potential of the crude extract of the endophyte *Daldinia eschscholtzii* (Ehrenb.) Rehm*,* isolated from the bark of the medicinal plant *Clausena excavata* Burm.f*.* The endophytic fungus was identified using morphological, microscopic, and molecular (ITS sequencing) methods, and small-scale cultivation was performed following a standard isolation protocol to obtain the crude extract. Phytochemical profiling of the crude extract was performed by GC-MS, and the brine shrimp lethality bioassay was used to assess preliminary cytotoxicity. Further, major metabolites identified by GC-MS were subjected to a network pharmacology-based *in-silico* ADMET analysis to predict their potential molecular targets and molecular mechanisms associated with prostate, ovarian, and breast cancer. The fungal extract exhibited significant cytotoxicity in the brine shrimp lethality bioassay. A total of thirty-seven fungal metabolites were identified by GC-MS. Network pharmacology analysis identified 31, 24, and 53 common target genes shared by the five major fungal metabolites and prostate, ovarian, and breast cancer, respectively. The PPI network identified AKT1, EGFR, STAT3, ESR1, HSP90AA1, PPARG, PTGS2, and EP300 as highly potential targets. The common genes were significantly associated with GO-enriched biological processes and 155 KEGG pathways, including ovarian, prostate, and breast cancer, EGFR, and STAT. Further, molecular docking studies revealed docking scores ranging from -6.6 to -8 kcal/mol. Among them, 1,8-dimethoxynaphthalene, methylhexadecanoate, and 4-methoxy-1-naphthalenol exhibited promising binding affinities toward AKT1, ESR1, HSP90AA1, and PPARG. Moreover, these metabolites demonstrated drug-like properties by following Lipinski's rule and favorable ADME profile with no predicted hepatotoxicity, nephrotoxicity, or cardiotoxicity. Our study links the *in-vitro* and *in-silico* cytotoxic activities of the drug-like constituents of the endophyte *D. eschscholtzii* by elucidating the molecular mechanisms underlying their potential anticancer effects against prostate, ovarian, and breast cancers.

Author contributions: Conceptualization, Nazia Hoque; Methodology, Nurun Nahar and Sk. Salman Araf; Software, Nurun Nahar and Sk. Salman Araf; Validation, Nurun Nahar and Nazia Hoque; Formal analysis, Nazia Hoque; Investigation, Nurun Nahar and Sk. Salman Araf; Writing - original draft, Nurun Nahar and Sk. Salman Araf; Writing - review and editing, Nazia Hoque; Supervision, Nazia Hoque; Project administration, Nazia Hoque; Funding acquisition, Nazia Hoque;



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Sciforum-210650: Could Teas and Refreshing Beverages Based on Sage Help Prevent Gingivitis? An *In Silico* Molecular Docking Study

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Sage (*Salvia officinalis* L.) has been used for centuries in traditional medicine in Serbia to treat inflammatory conditions of the oral cavity. Gingivitis is a common inflammatory condition primarily associated with bacterial dental plaque, causing redness, swelling, and gingival bleeding. Among bacteria associated with gingival inflammation, *Fusobacterium nucleatum* has been consistently linked to gingivitis, while *Aggregatibacter actinomycetemcomitans* has also been implicated.

Molecular docking was employed to investigate the binding affinity of rosmarinic acid and caffeic acid, two important polyphenolic compounds present in aqueous sage extract, to carboxypeptidase from *F. nucleatum* (PDB ID: 7EP9), whose inactivation could potentially affect peptide utilization and, consequently, the metabolic fitness of *F. nucleatum*, and de-N-acetilaza from *A. actinomycetemcomitans* (PDB ID: 4U10), whose inhibition could potentially impair the formation and maintenance of the bacterial biofilm, using chlorhexidine as a conventional oral antiseptic comparator.

The results revealed distinct predicted binding preferences. For 7EP9, caffeic acid showed the most favorable predicted binding potency (ΔG_{bind} = -6.02 kcal mol^{-1}; K_i = 38.76 μM), followed by rosmarinic acid (ΔG_{bind} = -5.79 kcal mol^{-1}; K_i = 57.46 μM), whereas chlorhexidine showed unfavorable binding (ΔG_{bind} = +24.11 kcal mol^{-1}). For 4U10, rosmarinic acid showed the most favorable predicted binding potency (ΔG_{bind} = -7.65 kcal mol^{-1}; K_i = 2.47 μM), followed by caffeic acid (ΔG_{bind} = -6.28 kcal mol^{-1}; K_i = 24.89 μM) and chlorhexidine (ΔG_{bind} = -5.69 kcal mol^{-1}; K_i = 67.02 μM). Complex stabilization involved predominantly conventional hydrogen bonds, together with carbon–hydrogen, π-donor hydrogen bonds, and other π-related interactions.

The docking results provide a preliminary molecular basis for interactions of caffeic and rosmarinic acids with bacterial proteins, requiring experimental validation. Chlorhexidine showed target-dependent interactions, suggesting potentially different mechanisms of antibacterial action. Based on their long-standing traditional use, sage-based teas and beverages may contribute to oral health and gingivitis prevention.

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Sciforum-210696: Beyond Bioactivity: Conformational Effects on the Electronic and Optical Properties of the Anti-Inflammatory Alkaloid Oleradiazahyde

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Introduction

Oleradiazahyde is a recently reported alkaloid with anti-inflammatory activity. It was isolated from *Portulaca oleracea*, an edible and medicinal plant widely distributed in tropical and subtropical regions and long used in traditional medicine. The flexible hydroxyethyl substituent of oleradiazahyde raises a question concerning its molecular characterization: to what extent can a single geometry represent its electronic and optical behavior in aqueous solution? This study investigates the effects of conformational heterogeneity on these properties.

Methods

An extensive GOAT/GFN2-xTB/ALPB(water) search generated 268 candidate structures, which were clustered into nine representatives. These structures were optimized using r^2SCAN-3c/SMD(water) and PBE0-D4/def2-TZVP/SMD(water), and both DFT levels produced the same energetic ordering. Harmonic frequency calculations verified the six lowest PBE0 conformers as minima. TD-PBE0/def2-TZVP calculations and natural transition orbital (NTO) analysis were performed for the three dominant conformational families.

Results

The six lowest conformers are distributed among three dominant families with estimated populations of approximately 75, 20, and 5%. Conformational variation substantially changes the molecular dipole moment, which ranges from 1.21 to 4.54 D, while the Kohn–Sham HOMO–LUMO gap varies only from 3.21 to 3.29 eV. The weak lowest singlet excitation occurs between 527 and 556 nm (f = 0.014–0.028). By contrast, a stronger fourth singlet transition remains between 279 and 283 nm (f = 0.306–0.326) and is dominated by a single NTO pair in all three families.

Conclusions

Conformational heterogeneity has a pronounced effect on the ground-state polarization of oleradiazahyde, but a more limited influence on its frontier-orbital gap and stronger UV transition. The results indicate that different electronic and optical properties respond differently to conformational rearrangement and provide an ensemble-based description of the physicochemical behavior of this recently identified bioactive natural product.



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Sciforum-210724: Mechanisms of Naoxueshu in spontaneous intracerebral hemorrhage: an integrative analysis of gut microbiota and network pharmacology

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This study systematically investigated the mechanisms underlying the therapeutic effects of Naoxueshu (NXS) on spontaneous intracerebral hemorrhage (sICH) by integrating gut microbiota analysis with network pharmacology strategies. Through database mining and literature screening, seven bioactive compounds of NXS were identified, along with 537 corresponding targets. A total of 80 sICH-related targets were retrieved from multiple disease-associated gene and target databases. Furthermore, 1,248 gut microbiota metabolite targets were obtained from the gutMGene database, and intersection analysis identified 18 overlapping targets shared among NXS, sICH, and the gut microbiota. A protein–protein interaction (PPI) network was constructed based on the intersecting targets, followed by enrichment analysis. Through bioinformatics analysis of the gut microbiota–pathway–target–compound network, the TLR4-mediated NF-κB signaling pathway was identified as a key pathway. Subsequently, ten core targets were identified using Cytoscape, and differential expression analysis of these targets in the intracerebral hemorrhage patient dataset GSE125521 from the Gene Expression Omnibus (GEO) database revealed three core targets with significantly altered expression. Molecular docking was then performed to validate the binding of active NXS components to these core targets, all of which exhibited favorable binding affinities. Analysis of the gutMGene database identified six potentially beneficial gut bacteria, including *Faecalibacterium prausnitzii* and *Lacticaseibacillus rhamnosus*. Finally, two key compounds were identified: 1,8-dihydroxy-3-hydroxymethylanthraquinone and 9,10-dimethoxypterocarpan-3-O-β-D-glucoside. These compounds were shown to comply with Lipinski's rule of five. Collectively, our findings demonstrate that NXS can modulate gut microbial homeostasis and intervene in the progression of sICH through multiple pathways, and that the core active compounds hold promise as candidate drug molecules for sICH.



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Sciforum-210767: Investigating the Potential of *Morus alba* and *Morus nigra* Extracts in Mitigating Anxiety in the Scopolamine-Treated Zebrafish Model

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Cognitive decline, memory impairment, and severe deterioration of the central cholinergic system characterize Alzheimer's disease. Alongside these deficits, patients frequently experience neuropsychiatric symptoms, particularly anxiety, which accelerates disease progression. Natural polyphenols are increasingly investigated to mitigate both cognitive and behavioral manifestations of neurodegeneration. Leaves of *Morus alba* and *Morus nigra* contain bioactive compounds with documented antioxidant and neuroprotective properties. Phytochemical profiling by RP-UHPLC-PDA analysis revealed polyphenols and flavonoids in both hydroalcoholic extracts, with *Morus nigra* showing higher overall polyphenol levels. Key identified compounds included chlorogenic acid, caffeic acid, hyperoside, luteolin-7-glucoside, and t-ferulic acid. This study evaluated the anxiolytic effect of hydroalcoholic leaf extracts (MAE and MNE) and morin in adult zebrafish (*Danio rerio*) with scopolamine-induced cholinergic dysfunction. Zebrafish were exposed daily via immersion for eight days to low (1 µg/L) and high (10 µg/L) concentrations of MAE or MNE, or morin (20 µM). Scopolamine (100 µM) was administered thirty minutes prior to behavioral testing, with imipramine (71 µM) as positive control. Exploratory behavior and anxiety were quantified using the Novel Tank Diving Test (NTT). Scopolamine induced a sharp increase in anxiety, significantly reducing time in the top tank section ($p < 0.00001$) and prolonging freezing duration ($p < 0.00001$). Treatments reversed these deficits dose-dependently. Higher concentrations (MAE-H, MNE-H) restored exploratory activity to levels comparable with imipramine. Total distance traveled remained unchanged, confirming specific anxiety reduction without motor impairment. In conclusion, *Morus alba* and *Morus nigra* extracts exhibit pronounced anxiolytic activity, representing relevant therapeutic options for anxiety associated with cholinergic neurodegeneration.



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Sciforum-210779: Fe_3O_4 nanoparticle-induced enhancement of phenolic acid and flavonoid content in cell suspension culture of *Scrophularia striata* Boiss.

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Stimulating secondary metabolite production in medicinal plants remains a major challenge, requiring innovative elicitation strategies. Plant cell culture provides a controlled platform for phytochemical production, particularly in *Scrophularia striata* Boiss., a medicinal species rich in secondary metabolite. Iron oxide nanoparticles (Fe_3O_4 NPs) are promising abiotic elicitors whose effects depend on concentration and exposure time. This study investigated the concentration- and time-dependent responses of *S. striata* cell suspension cultures to Fe_3O_4 NPs. Cells were exposed to different nanoparticle concentrations (5, 20, 50, 75, and 100 mg/L), followed by time-course analysis at the optimized concentration of 5 mg/L over 24-96 h. Phenolic acid and flavonoid profiles were quantified by HPLC, while antioxidant enzyme activities, oxidative stress markers, and total antioxidant capacity were evaluated. Fe_3O_4 NPs enhanced phenolic and flavonoid accumulation, accompanied by increased phenylalanine ammonia-lyase activities. *p*-coumaric acid showed the greatest increase at 5 mg/L, suggesting enhanced phenylpropanoid metabolism and PAL activity, whereas catechin exhibited the strongest flavonoid response, reaching its highest accumulation at 24 h, particularly at 5 mg/L. Other metabolites showed distinct concentration and time-dependent patterns, with several reaching maxima during 24-48 h, highlighting this period as a critical response window. The greatest efficacy occurred at 5 mg/L, where Fe_3O_4 NPs promoted defense-related metabolic responses without evident oxidative damage, consistent with a hormetic dose-response pattern. In contrast, higher concentrations increased oxidative stress and reduced biosynthetic activity. These findings highlight importance of optimizing nanoparticle concentration and exposure duration to enhance the sustainable production of valuable specialized metabolites in *S. striata* cultures.

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Sciforum-210785: In Silico Investigation of Naringenin Binding to COX-2: Docking, Molecular Dynamics, and Comparison with COX-1

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Naringenin, a citrus-derived flavanone, was investigated using computational methods to characterize its predicted binding to cyclooxygenase-2 (COX-2), a target associated with inflammatory signaling and cancer-related biology, and to compare its interactions with COX-1. Molecular docking using AutoDock Vina yielded a predicted affinity of -9.47 kcal/mol for naringenin against human COX-2 (PDB ID: 5KIR), whereas the reference inhibitor rofecoxib showed a more favorable score of -10.15 kcal/mol under the same docking conditions. Redocking across three independent seeded runs reproduced the crystallographic rofecoxib pose, with a mean heavy-atom RMSD of 0.92 ± 0.001 Å (mean ± SD), supporting the ability of the selected protocol to reproduce the reference ligand pose. Docking to human COX-1 (PDB ID: 6Y3C) yielded less favorable scores; relative to COX-1, the COX-2 score was more favorable by 1.31 kcal/mol for naringenin and 2.82 kcal/mol for rofecoxib. Twenty-nanosecond explicit-solvent molecular dynamics simulations in GROMACS, using the AMBER99SB-ILDN protein force field and explicitly described ligand parameters, yielded mean backbone RMSDs of 0.128 and 0.191 nm for the naringenin–COX-2 and naringenin–COX-1 complexes, respectively. Ligand RMSD, ligand–binding-site minimum-distance analysis, and trajectory inspection suggested intra-pocket reorientation without observed dissociation during the simulated interval. MM-GBSA calculations yielded more favorable approximate binding-energy estimates for COX-2 than for COX-1 (-23.51 versus -20.16 kcal/mol), although these estimates should not be interpreted as experimentally determined free energies. In silico ADME profiling using SwissADME predicted high gastrointestinal absorption, no violations of the Lipinski, Ghose, Veber, Egan, and Muegge drug-likeness rules, and no PAINS or Brenk alerts. Overall, the computational results suggested a more favorable predicted interaction of naringenin with COX-2 than with COX-1 under the modeled conditions. Experimental enzyme-inhibition assays against both isoforms are required to determine whether this predicted preference corresponds to biochemical selectivity.



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Sciforum-210826: Dynamics of accumulation of phenolic compounds and flavonoids in the leaves of two apricot cultivars (*Prunus armeniaca* L.) during the vegetation period.

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Background. Apricot (Prunus armeniaca L.) leaves are an underexplored plant material rich in secondary metabolites with known antioxidant and health-promoting effects. Although apricot leaf extracts are gaining attention for nutraceutical use, data on how phenolic composition varies between cultivars and across the growing season remain limited. **Objective.** This study investigated the seasonal accumulation patterns of total phenolics and flavonoids in leaves of two P. armeniaca cultivars grown under the same agroecological conditions. **Materials and Methods.** Leaf samples from two apricot cultivars were collected every two weeks from a single orchard in Armenia throughout the vegetation season (eight sampling points per cultivar). Phenolic compounds were extracted with 70% (v/v) ethanol using ultrasound-assisted extraction. Total phenolic content (TPC) was measured spectrophotometrically with the Folin–Ciocalteu reagent and expressed as mg gallic acid equivalents per g dry weight (mg GAE/g DW). Total flavonoid content (TFC) was determined by the aluminum chloride colorimetric method and expressed as mg rutin equivalents per g dry weight (mg RE/g DW).

Results. TPC ranged from 13.27 to 37.24 mg GAE/g DW, with the highest values observed during fruit development in May. TFC varied between 16.62 and 27.06 mg RE/g DW, also peaking in May. Significant differences between cultivars were found ($p < 0.05$). Cultivar Shalakh showed higher total phenolic content than Tabarza, with a peak in May. In contrast, Tabarza reached maximal phenolic levels in late July, after fruiting. For flavonoids, Shalakh had higher levels only at the start of fruiting, while Tabarza accumulated more flavonoids overall, with a peak during fruit development in June. **Conclusion.** Apricot leaf phenolics show clear seasonal and cultivar-specific variation, with early-to-mid vegetation stages offering the best harvest window for maximizing bioactive compound yield. These results support the use of apricot leaves as a sustainable raw material for dietary supplements and functional foods.



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Sciforum-210827: Development of natural chlorin-based photoactivatable Pt(II) and Pt(IV) complexes.

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Platinum-based chemotherapeutic agents are widely used in the treatment of various solid tumors. However, Pt(II) compounds have a number of limitations, such as insufficient selectivity of accumulation and action, which leads to numerous adverse effects. It is also known about drug resistance of tumor cells, resulting in reduced platinum accumulation and activation of DNA repair systems. The development of novel platinum-based anticancer agents remains a critical challenge in modern medicinal chemistry.

Unlike Pt(II) complexes, Pt(IV) compounds are kinetically inert and can serve as prodrugs. Upon reduction within the cell by intracellular reducing agents (glutathione, ascorbic acid) or by exposure to light of a specific wavelength, Pt(IV) complex releases not only the cytotoxic moiety but also two axial ligands, which may themselves possess biological activity.

Another strategy to minimize side effects involves the use of photocaged molecules in therapy. This approach significantly enhances the selectivity and efficacy of cancer treatment while reducing systemic toxicity through targeted activation of the molecule at the lesion site.

This study focuses on the development of photoactivatable Pt(II) and Pt(IV) complexes using natural chlorin-based photosensitizers as vector molecules characterized by high affinity for tumor tissue. The obtained compounds were analyzed using a set of physicochemical methods (NMR spectroscopy, mass-spectrometry, studies on determining the quantum yield of singlet oxygen and LogP), and their structures were reliably confirmed by high-resolution chromatography–mass spectrometry. At the current stage, primary in vitro cytotoxicity studies and intracellular accumulation are being evaluated using the A549 lung adenocarcinoma cell line.

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Sciforum-210849: Minimal Concentrations of a Chemically Modified Triterpene Derivative of Ursolic Acid (UA) Rapidly Exterminate MDR HR-NB HTLA Cells, Outperforming UA and Etoposide

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Late-stage metastatic high-risk neuroblastoma (HR-NB) childhood cancer has $<$ 50% survival rates, due to the emergence of resistance to available therapies, generally based on etoposide (ETO), doxorubicin (DOX), etc. Aiming at ameliorating this worrying scenario, 7 triterpenoid derivatives (**1**-**7**) were synthesized, decorating betulin (BET), betulinic acid (BA) and ursolic acid (UA). They were essayed on sensitive MYCN-amplified HTLA 230 cells and multidrug resistant (MDR) HTLA ER counterpart, known to be the most aggressive forms of HR-NB, regardless their phenotype. All compounds displayed from moderate to potent anticancer effects, but the anticancer potency of UA derivative **7**, was exceptional. Specifically, **7** demonstrated potent activity against both cell lines (IC_{50} = 1.75-0.58 vs. HTLA 230 and 4.30-2.90 μM vs. HTLA ER), eliciting up to sub micromolar concentrations, in 72h experiments. UA derivative **7** was superior to UA by 25.3-60.5- (HTLA 230) and 8.6-9.4-time (HTLA ER), and outperformed both UA and ETO already in 24h treatments by 8.4-58.9-fold (UA) and by 83.1-118.8-fold (ETO). Since, these incomparable discoveries recognised **7** as worthy of further experiments, clonogenicity tests, kinases phosphorylation investigations were performed. Clonogenicity was fully suppressed at all concentration tested in HTLA 230, while at the minimal concentration tested in HTLA ER, while kinase phosphorilation tests and the quantification of other markers evidenced that cytotoxicity of **7** was based on the inhibition of the AkT kinase system, due to the presence of acetylenic triple bond.

Author contributions: Conceptualization, Silvana Alfei, Barbara Marengo and Cinzia Domenicotti; Methodology, Barbara Marengo and Cinzia Domenicotti; Software, Barbara Marengo and Cinzia Domenicotti; Validation, Barbara Marengo; Formal analysis, Silvana Alfei and Barbara Marengo; Investigation, Silvana Alfei and Barbara Marengo; Resources, Cinzia Domenicotti; Data curation, Silvana Alfei and Barbara Marengo; Writing - original draft, Silvana Alfei; Writing - review and editing, Silvana Alfei and Barbara Marengo; Supervision, Silvana Alfei and Cinzia Domenicotti; Project administration, Silvana Alfei and Cinzia Domenicotti;



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Sciforum-210896: Phytochemical Screening, Chromatographic Profiling and Bioactivity Evaluation of *Gardenia fosbergii* Fruit Extract

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The present study aimed to evaluate the phytochemical screening and chromatographic profiing of sequentially extracted chloroform, petroleum ether, carbon tetrachloride and methanol fractions derived from ripe fruit of *Gardenia fosbergii Tirveng.* (family Rubiaceae). Selected biological activities of *G. fosbergii* fruit extract were reported for the first time in this study. The phytochemical analysis of fruit fractions obtained from four organic solvents was carried out to determine the bio-active compounds such as alkaloids, flavonoids, terpenoids, steroids and phenolics. Total Phenolic Content (TPC) was highest for some fractions at 500 µg/mL (e.g., 750.33 mgGAE/g), with lower amounts observed at 1000 µg/mL. TLC profiling elucidated component separation, while column chromatography facilitated their isolation and purification for further structural characterization. Biological assays revealed significant antimicrobial, insecticidal, radical scavenging and cytotoxic activities supporting the therapeutic potential of *G. fosbergi*i. Antimicrobial activity, tested against *E. coli, S. aureus, P. aeruginosa,* and *Candida sp.* by disc diffusion method showed greater efficacy at 1000 mg/mL than at 500 mg/mL. Insecticidal activity was conducted using *Culex quinquefasciatus* larvae against 0.25 – 2 mg/mL concentrations. The susceptibility of larvae in the order; Pet –Ether (45%) $>$ Chloroform $>$ Methanol $>$ Carbon tetrachloride (20%). Cytotoxicity against *Artemia salina* nauplii followed the order: Chloroform (80%) $>$ Pet-Ether $>$ Methanol $>$ Carbon tetrachloride (56%). DPPH radical scavenging activity was dose dependent, yielding IC_{50} values of 13.27, 101.84, 227.03, and 243.81 µg/mL for the respective fractions, compared to the internal standard, ascorbic acid (55.27 µg/mL). Results were statistically analyzed using one way ANOVA and Tukey's test ($P < 0.05$). These findings underscore the significant therapeutic potential of *G. fosbergii* fruit extract and support its promising applications in the development of novel therapeutic interventions.

Author contributions: Conceptualization, Joy Ebenezer Rajakulendran and Umaramani Mathiventhan; Methodology, Vimashi Geethmi Hewagamage, Joy Ebenezer Rajakulendran and Umaramani Mathiventhan; Formal analysis, Joy Ebenezer Rajakulendran and Umaramani Mathiventhan; Investigation, Vimashi Geethmi Hewagamage; Resources, Joy Ebenezer Rajakulendran and Umaramani Mathiventhan; Data curation, Vimashi Geethmi Hewagamage; Writing - original draft, Vimashi Geethmi Hewagamage; Writing - review and editing, Joy Ebenezer Rajakulendran and Umaramani Mathiventhan;



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Sciforum-210927: Licochalcone A Attenuates Acute Lung Injury through Modulation of STING Signaling and Mitochondrial Quality Control

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Acute lung injury (ALI) is characterized by excessive inflammatory responses and mitochondrial dysfunction, yet effective pharmacological interventions remain limited. Aberrant activation of the cyclic GMP–AMP synthase–stimulator of interferon genes (cGAS–STING) pathway has emerged as an important contributor to inflammatory tissue injury. Licochalcone A (LCA), a bioactive chalcone derived from licorice, possesses broad anti-inflammatory activity, but its molecular basis in ALI remains incompletely understood. In this study, we investigated whether LCA protects against ALI by modulating STING-associated inflammatory signaling and mitochondrial homeostasis. Target-prediction, computational, and cellular target-engagement analyses supported STING as a molecular target of LCA. LCA attenuated STING activation and downstream TBK1–IRF3/NF-κB signaling, accompanied by reduced inflammatory responses in macrophages and improved pulmonary injury in an LPS-induced mouse model. Further analyses showed that LCA alleviated mitochondrial dysfunction and restored cellular quality-control processes associated with lysosomal function and mitophagy. Collectively, these findings identify LCA as a natural small-molecule modulator of STING signaling and suggest that coordinated regulation of inflammatory signaling and mitochondrial homeostasis contributes to its protective effects against ALI. LCA may therefore provide a promising natural-product scaffold for the development of STING-targeted therapeutics.



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Sciforum-210935: Assessment of antioxidant activity of Phloretin and Neohesperidin Dihydrochalcone and their mixture using New Approach Methodologies (NAMs)

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Ultraviolet (UV) radiation generates reactive oxygen species (ROS), triggering skin inflammation, activating AP-1, increasing matrix metalloproteinase (MMP) expression, and inhibiting collagen synthesis, ultimately promoting extracellular matrix degradation and photoaging. New Approach Methodologies (NAMs), including human cell-based in vitro assays, provide relevant non-animal tools for evaluating the biological activity of cosmetic ingredients. The aim of this study was to assess the antioxidant of two natural compounds (Phloretin, NF02; and Neohesperidin dihydrochalcone, NHDC), individually and in combination, and to investigate possible synergistic effects. UV-Vis absorption spectra were obtained according to OECD 101 (1981). Cytotoxicity was evaluated in HaCaT keratinocytes (Eucellbank, Celltec–Universitat de Barcelona) exposed to 10–100 µg/mL of each compound or their mixture for 24 h using the Neutral Red Uptake (NRU) and MTT assays. Intracellular ROS production was determined after treatment with 10 or 20 µg/mL of the compounds followed by UVA irradiation (10 J/cm^2). DCFH-DA was used as the fluorescent probe, and fluorescence values were normalized to cellular protein content determined by the Bradford assay. N-acetyl-L-cysteine and untreated cells were included as positive and negative antioxidant controls, respectively. MTT results showed an IC50 of approximately 100 µg/mL, whereas no IC_{50} could be determined with the NRU assay. All compounds exhibited high molar extinction coefficients. Both individual compounds and their combination significantly reduced UVA-induced ROS production, with the mixture producing the greatest inhibition, suggesting a synergistic antioxidant effect. These findings support the usefulness of NAMs for the characterization of bioactive cosmetic ingredients.

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Author contributions: Conceptualization, Adriana Solange Maddaleno, Maria Pilar Vinardell, Judit Camargo and Montse Mitjans Arnal; Methodology, Adriana Solange Maddaleno and Montse Mitjans Arnal; Formal analysis, Adriana Solange Maddaleno, Maria Pilar Vinardell and Montse Mitjans Arnal; Investigation, Adriana Solange Maddaleno, Maria Pilar Vinardell, Judit Camargo and Montse Mitjans Arnal; Resources, Judit Camargo; Data curation, Adriana Solange Maddaleno and Montse Mitjans Arnal; Writing - original draft, Adriana Solange Maddaleno and Montse Mitjans Arnal; Writing - review and editing, Adriana Solange Maddaleno, Maria Pilar Vinardell and Montse Mitjans Arnal; Supervision, Judit Camargo and Montse Mitjans Arnal; Project administration, Judit Camargo; Funding acquisition, Judit Camargo and Montse Mitjans Arnal;



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Sciforum-210943: Antioxidant Potential of Oil Shrimp Shells Extracts

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Introduction: Shrimp shells are an abundant by-product of the seafood industry and are frequently discarded, contributing to environmental concerns. Nevertheless, they contain valuable bioactive compounds with potential antioxidant properties. This study aimed to evaluate the antioxidant activity of shrimp shell extracts obtained using sunflower oil and to assess their potential as sustainable sources of natural antioxidants.

Methods: Shrimp shells were collected, cleaned, dried, and subjected to ultrasound-assisted extraction using sunflower oil as the extraction medium. The antioxidant activity of the resulting extracts was evaluated using the DPPH and ABTS radical scavenging assays. Results were expressed as percentage of radical scavenging activity and compared with ascorbic acid used as a reference antioxidant.

Results: The shrimp shell extracts demonstrated substantial radical scavenging activity at the tested concentrations. In the DPPH assay, the extract showed 82.15 ± 0.33% radical scavenging activity at 5.4 µg/mL, whereas ascorbic acid reached 31.75 ± 0.84% at the same concentration. In the ABTS assay, the extract exhibited 51.78 ± 0.31% radical scavenging activity at 3.90 µg/mL, compared with 44.61 ± 0.92% for the reference antioxidant at the same concentration.

Conclusions: These findings highlight the antioxidant potential of shrimp shell extracts obtained using sunflower oil and support the valorization of shrimp-processing by-products as sources of natural bioactive compounds. The results provide a basis for further development of these extracts through their incorporation into nanostructured lipid carriers (NLC), with the aim of exploring their potential for cosmetic applications.



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Sciforum-210998: In vitro evaluation of the anti-inflammatory and thrombolytic properties of *Aidia densiflora* (Wall.) Masam. *stems*

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Natural products are the reservoirs of bioactive constituents providing various therapeutic applications in inflammation and thrombosis-related conditions. The pharmacological effects of *Aidia densiflora* (Wall.) Masam., a medicinal species belonging to the Rubiaceae family remain unidentified. This study investigated *in vitro* anti-inflammatory and thrombolytic properties of the methanolic extract of *Aidia densiflora* (Wall.) Masam. stems. Anti-inflammatory effect of the extract was evaluated by protein denaturation assay and thrombolytic effect was measured by human blood clot lysis method.

Aidia densiflora (Wall.) Masam. demonstrated significant concentration-dependent anti-inflammatory activity, with a maximum inhibition of 83.05 ± 1.39% at 1000 µg/mL, compared with the standard drug, diclofenac sodium at the same concentration. The extract also showed moderate thrombolytic activity by producing 22.09 ± 1.29% clot lysis, which was markedly higher than the negative control but substantially lower than the standard (streptokinase). Streptokinase exhibited a marked clot lysis activity (72.71 ± 0.70%), whereas the control showed negligible clot lysis (9.16 ± 0.35%).

Due to its potent anti-inflammatory and moderate thrombolytic effects, stems of *Aidia densiflora* (Wall.) Masam. might be considered for the drug development of the alternative medicine against inflammation and thrombotic disorders.

Author contributions: Conceptualization, Sharmin Noor and Tasnim Rahman; Methodology, Sharmin Noor and Tasnim Rahman; Software, Sharmin Noor; Validation, Shukranul Mawa; Formal analysis, Sharmin Noor; Investigation, Sharmin Noor and Tasnim Rahman; Resources, Shukranul Mawa and Tasnim Rahman; Data curation, Sharmin Noor and Shukranul Mawa; Writing - original draft, Sharmin Noor; Writing - review and editing, Shukranul Mawa; Visualization, Shukranul Mawa; Supervision, Shukranul Mawa; Project administration, Shukranul Mawa;



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Sciforum-211031: SKF7® Attenuates Lipid Accumulation in HepG2 Cells: Potential Implications for Menopause-Associated Metabolic Dysfunction

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Menopause-associated metabolic dysfunction is characterized by increased lipid accumulation, obesity, and an elevated risk of non-alcoholic fatty liver disease, driven by hormonal imbalance and altered lipid metabolism. Hepatic lipid accumulation is a key feature of metabolic dysfunction and can be modelled in vitro using free fatty acid (FFA)-induced HepG2 cells. SKF7®, a standardized aqueous ethanolic extract of *Labisia pumila*, has emerged as a promising botanical product with lipid-lowering properties. This study aimed to evaluate the effects of SKF7® on hepatic lipid accumulation in HepG2 cells and its potential relevance to menopause-associated metabolic dysfunction. The cytotoxicity of SKF7® (10–1000 µg/ml) was evaluated using the MTT assay. Based on cell viability, concentrations ≤250 µg/ml were selected for subsequent experiments. Hepatic lipid accumulation was induced using sodium oleate (SO) at 0.5 and 1.0 mM conjugated with 1% bovine serum albumin. Preliminary findings identified 1.0 mM SO as the optimal concentration for lipid accumulation. FFA-induced HepG2 cells were subsequently treated with SKF7® for 24 h, and intracellular lipid accumulation was assessed using Oil Red O staining. SKF7® showed no significant cytotoxicity at concentrations ≤250 µg/ml. SKF7® treatment significantly attenuated intracellular lipid accumulation in FFA-induced HepG2 cells, with the most pronounced reduction observed at 250 µg/ml compared with the FFA-induced control group ($p < 0.001$). Notably, lipid accumulation at 250 µg/ml was not significantly different from the untreated normal group. These findings demonstrate that SKF7® attenuates hepatic lipid accumulation, supporting its potential role in improving hepatic lipid homeostasis and menopause-associated metabolic dysfunction.

Author contributions: Conceptualization, Elda Nurafnie Ibnu Rasid; Methodology, Elda Nurafnie Ibnu Rasid; Formal analysis, Elda Nurafnie Ibnu Rasid; Investigation, Elda Nurafnie Ibnu Rasid; Writing - original draft, Elda Nurafnie Ibnu Rasid;



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Sciforum-211090: Gastroprotective Effect of Costus afer Stem Methanol Extact on HCL/Ethanol-Induced Gastric Ulcer in Albino Rats

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Gastric ulcer remains a significant gastrointestinal disorder, with disruption of the gastric mucosal barrier and imbalance between aggressive and protective factors contributing to ulcer development. The limitations associated with conventional anti-ulcer therapies have increased interest in medicinal plants as potential sources of gastroprotective agents. This study investigated the gastroprotective activity of methanolic stem extract of *Costus afer* against HCl/ethanol-induced gastric ulcer in Wistar rats. Twenty-four Wistar rats were randomly assigned to six groups (n = 4) and pretreated with vehicle, lansoprazole (30 mg/kg), or *C. afer* extract (200, 400, and 600 mg/kg body weight) for seven days before ulcer induction.Preliminary phytochemical screening and acute oral toxicity testing were conducted, while gastric juice volume, gastric pH, ulcer index, percentage ulcer protection, and histopathological changes were evaluated.Preliminary screening indicated that the extract contained alkaloids, flavonoids, terpenoids, glycosides, saponins, and tannins, with no mortality observed up to 5000 mg/kg. HCl/ethanol increased gastric juice volume and reduced gastric pH. Pretreatment with *C. afer* reduced gastric juice volume to 1.71, 1.57, and 1.44 mL and increased gastric pH to 7.33, 7.55, and 8.02 at 200, 400, and 600 mg/kg, respectively. Ulcer protection increased dose-dependently to 40.34%, 52.44%, and 69.16%, compared with 50.43% for lansoprazole. Histopathology showed reduced mucosal damage, particularly at 600 mg/kg. These findings suggest that methanolic stem extract of *C. afer* possesses gastroprotective activity and warrants further investigation, including detailed phytochemical characterization using specific analytical techniques.

Author contributions: Conceptualization, Chinelo Mercy Ugwu and Ugochi Olivia Njoku; Methodology, Chinelo Mercy Ugwu and Ugochi Olivia Njoku; Validation, Ugochi Olivia Njoku; Formal analysis, Chinelo Mercy Ugwu; Investigation, Chinelo Mercy Ugwu; Data curation, Chinelo Mercy Ugwu; Writing - original draft, Chinelo Mercy Ugwu; Writing - review and editing, Chinelo Mercy Ugwu and Ugochi Olivia Njoku; Supervision, Ugochi Olivia Njoku;



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Sciforum-211099: Network Pharmacology and Molecular Docking-Based Investigation of Tectoquinone Against Non-Alcoholic Fatty Liver Disease

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Background: Non-alcoholic fatty liver disease (NAFLD) is a metabolic liver disorder associated with hepatic lipid accumulation, oxidative stress, inflammation and altered cellular signaling. Tectoquinone, a naturally occurring phytoconstituent, may possess potential activity against these pathological processes; however, its molecular mechanism in NAFLD remains insufficiently explored.

Objective: The present study aimed to identify potential targets and signaling pathways of tectoquinone associated with NAFLD and to evaluate its interaction with key hub proteins using molecular docking.

Methods: SwissADME was used to evaluate the physicochemical and drug-likeness properties of tectoquinone, while ProTox-3.0 was employed for toxicity prediction. Potential drug targets were obtained from SwissTargetPrediction, and NAFLD-associated targets were retrieved from GeneCards. Venny analysis identified 44 common targets between tectoquinone and NAFLD. Gene Ontology and KEGG pathway enrichment analyses were performed, followed by construction of a drug–pathway–gene network using Cytoscape. Network analysis identified five major hub targets: ESR1, CTNNB1, BCL2, NFE2L2 and GSK3B. Molecular docking was subsequently performed with selected hub proteins.

Results: Tectoquinone showed favorable drug-likeness characteristics and high gastrointestinal absorption, with no major toxicity predicted in the evaluated ProTox endpoints. Enrichment analysis indicated involvement of multiple pathways related to metabolic regulation, lipid metabolism, inflammation and cellular signaling. Molecular docking demonstrated binding affinities of -10.0 kcal/mol with BCL2, -6.9 kcal/mol with CTNNB1, and approximately 0.0 kcal/mol with ESR1. Among the evaluated proteins, BCL2 exhibited the strongest predicted binding affinity (-10.0 kcal/mol).

Conclusion: These findings suggest that tectoquinone may interact with multiple NAFLD-associated targets, with BCL2 emerging as the most promising docked target, warranting further experimental validation.

Author contributions: Conceptualization, Pavan Bhausaheb Udavant; Methodology, Pavan Bhausaheb Udavant and Vaishnavi Tushar Mahajan; Resources, Vaishnavi Tushar Mahajan; Writing - original draft, Vaishnavi Tushar Mahajan; Writing - review and editing, Pavan Bhausaheb Udavant; Supervision, Pavan Bhausaheb Udavant;



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Sciforum-211121: Isolation and Screening of Bacteria with Biotechnological Potential from Permafrost-Associated Soils of Northern Pakistan

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Soil microorganisms from high-altitude and cold environments represent an important source of biotechnologically valuable enzymes and antimicrobial compounds. The present study investigated the bacterial diversity and selected biotechnological potential of soil microorganisms isolated from the northern areas of Pakistan, including soil collected from Babusar Top, an area associated with documented permafrost soils in the Babusar Valley, and Rainbow Bridge. Soil samples were subjected to serial dilution and culture-based isolation, followed by morphological, Gram-staining, biochemical, antimicrobial, and extracellular enzyme screening. Growth from the Babusar Top sample was observed at the 10^{-2} dilution, from which four bacterial isolates (BS1, BS2, SB1 and SB2) were obtained, while two additional isolates (RB1 and RB2) were recovered from Rainbow Bridge. All six isolates were Gram-positive rods. Screening for cellulolytic activity showed growth of five isolates (SB2, BS1, BS2, RB1 and RB2; 83.3%) on carboxymethyl cellulose agar under the conditions tested. All six isolates (100%) produced clear zones on milk agar, indicating extracellular protease-mediated casein hydrolysis. Lipase screening showed growth of SB1, BS1, and RB2 (50%) accompanied by grainy precipitate-like appearances around colonies, although no clear hydrolysis zones were observed. All six isolates (100%) were positive for ammonification, demonstrated by a deep yellow color with Nessler's reagent. In antimicrobial screening, SB2 and RB1 (33.3%) produced inhibition against both *Escherichia coli* and *Staphylococcus aureus*, demonstrating activity against Gram-negative and Gram-positive test bacteria. These findings demonstrate that bacteria isolated from high-altitude northern Pakistani soils, including the documented permafrost-associated Babusar region, possess diverse enzymatic, metabolic, and antimicrobial properties with potential biotechnological applications.

Author contributions: Conceptualization, Rabia Tanvir; Methodology, Zarnab Gul; Formal analysis, Zarnab Gul; Investigation, Zarnab Gul; Resources, Rabia Tanvir; Data curation, Zarnab Gul; Writing - original draft, Rabia Tanvir; Writing - review and editing, Rabia Tanvir; Visualization, Rabia Tanvir; Supervision, Rabia Tanvir; Funding acquisition, Rabia Tanvir;



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Sciforum-211300: Natural Strategies for Skin Health: Bioactivity Profiling of *Plectranthus* Species with Antimicrobial and Skin-Related Enzyme Inhibitory Activities

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Plectranthus species have long been valued in traditional medicine for the management of skin-related disorders and are increasingly recognized as promising sources of bioactive compounds with dermatological relevance. Despite their widespread ethnopharmacological use, scientific validation of these properties remains scarce for several species. Therefore, the present study investigated the biological potential of eight *Plectranthus* species (*P. ambiguus* (Bolus) Codd, *P. barbatus* Andrews, *P. cylindraceus* (Hochst. ex Benth.) A.J. Paton, *P. ecklonii* Benth., *P. fruticosus* L'Hér., *P. grandidentatus* Gürke., *P. hadiensis*, *P. madagascariensis* Benth.) in order to substantiate their traditional uses and explore their suitability for dermatological applications.

To assess their biological activity, extracts were subjected to a comprehensive evaluation that included general toxicity testing using the *Artemia salina* lethality assay, antimicrobial screening, and the determination of inhibitory effects against enzymes closely associated with skin ageing and pigmentation processes, namely elastase, collagenase, and tyrosinase.

None of the tested extracts exhibited general toxicity in the *Artemia salina* model, indicating a favourable preliminary safety profile. Antimicrobial activity was mainly directed against Gram-positive bacteria, with *Staphylococcus* species showing the highest susceptibility. The enzymatic assays highlighted the anti-ageing potential of several extracts. Among them, *P. ecklonii* and *P. cylindraceus* displayed the most pronounced elastase inhibitory activity, with IC_{50} values of 62.82 and 84.76 µg/mL, respectively. Notably, *P. ecklonii* demonstrated greater inhibitory capacity than the reference compound kojic acid (IC_{50} = 75.55 µg/mL). In addition, extracts from *P. ecklonii*, *P. grandidentatus*, and *P. fruticosus* showed considerable collagenase inhibition, with IC_{50} values ranging from 86.62 to 95.93 µg/mL, suggesting their potential to the preservation of skin structure. Collectively, these results provide scientific support for the ethnopharmacological use of *Plectranthus* species and reinforce their potential as valuable natural sources of bioactive compounds for skin care applications.

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Sciforum-211330: Larvicidal activity of *Dialium cochinchinense* (Velvet Tamarind) fruit extract against mosquito larvae

Habibu Tijjani [1,*], Grace Chinyere Ambrose-Nnaji [2], Esther Iyabo Joseph [2], Toluhi Esther Bosede [2], Salima Adamu Sada [1], Oluremi A. Saliu [1], Suwaiba Nasir [1], Ayodeji O. Idowu [1], Shehu Usman Adamu [2] and Uchechi Susan Awuja-christopher [3]

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Dialium cochinchinense (Velvet tamarind) fruit is a medicinal plant important for management of diarrhoea, fever, microbial infections, palpitations, stomatitis and toothache. This study evaluated the larvicidal activities of *D. cochinchinense* fruit extract against mosquito larvae. Larvae were collected from Lugbu FCT-Nigeria and introduced into 10, 20, 40, 80 and 100 mg/mL of *D. cochinchinense* fruit extract. Azadirachtin (10 mg/mL), DMSO and Triton X100 were used as controls. Larvae mortality was monitored at 24, 48 and 72 hours. For pupae and mosquito emergence rate, the larvae were reared in the laboratory to pupae stage, and the rate of mosquito emergence was monitored. Larvae mortality ranged from 0.00±0.00% to 25.56±12.62% after 24 hours, increasing to 29.21±13.34% at 100 mg/mL after 48 hours and 52.06±24.66% at 100 mg/mL after 72 hours. Azadirachtin produced 61.11±34.69% mortality after 24 hours and 100% mortality after 48 and 72 hours respectively, while Triton X-100 (1%) caused complete mortality. The extract showed low to moderate pupaecidal activity. After 24 hours, mortality ranged from 0.00% to 15.28±2.41%, while after 48 hours the highest mortality was 29.76±18.33% at 40 mg/mL. Azadirachtin caused 9.70±1.01% pupae mortality at 24 hours and 19.39±1.05% at 48 and 72 hours, whereas Triton X-100 caused 100% pupae mortality throughout the experiment. At 24 hours, mosquito emergence ranged from 10.32±3.52% to 90.48±16.50%. Prolonged exposure did not increase inhibitory effects on mosquito emergence rate, with 20 mg/mL achieving 100% emergence at 48 and 72 hours respectively, while 10 mg/mL produced 94.44±9.62% emergence. *D. cochinchinense* extract demonstrated greater potential on larval mortality than inhibition of mosquito emergence. Aqueous *Dialium cochinchinense* fruit extract demonstrated promising mosquito-control potential, particularly by its larvicidal activities.

Author contributions: Conceptualization, Habibu Tijjani and Shehu Usman Adamu; Methodology, Habibu Tijjani, Grace Chinyere Ambrose-Nnaji, Esther Iyabo Joseph, Toluhi Esther Bosede, Salima Adamu Sada, Oluremi A. Saliu, Suwaiba Nasir, Ayodeji O. Idowu and Shehu Usman Adamu; Validation, Oluremi A. Saliu; Formal analysis, Habibu Tijjani, Grace Chinyere Ambrose-Nnaji, Esther Iyabo Joseph, Toluhi Esther Bosede, Salima Adamu Sada, Oluremi A. Saliu, Suwaiba Nasir and Ayodeji O. Idowu; Investigation, Habibu Tijjani, Grace Chinyere Ambrose-Nnaji, Esther Iyabo Joseph, Toluhi Esther Bosede, Suwaiba Nasir and Uchechi Susan Awuja-christopher; Resources, Habibu Tijjani, Grace Chinyere Ambrose-Nnaji and Salima Adamu Sada; Data curation, Habibu Tijjani, Grace Chinyere Ambrose-Nnaji, Esther Iyabo Joseph, Toluhi Esther Bosede, Suwaiba Nasir and Uchechi Susan Awuja-christopher; Writing - original draft, Habibu Tijjani, Grace Chinyere Ambrose-Nnaji, Esther Iyabo Joseph, Salima Adamu Sada and Uchechi Susan Awuja-christopher; Writing - review and editing, Habibu Tijjani, Toluhi Esther Bosede, Oluremi A. Saliu, Suwaiba Nasir, Ayodeji O. Idowu and Shehu Usman Adamu; Visualization, Habibu Tijjani; Supervision, Habibu Tijjani, Ayodeji O. Idowu and Shehu Usman Adamu; Project administration, Habibu Tijjani, Salima Adamu Sada, Oluremi A. Saliu, Ayodeji O. Idowu and Shehu Usman Adamu;



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Sciforum-211331: Synthesis and Antiproliferative Evaluation of a New Formyl Derivative of Carnosic Acid

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The abietane-type diterpenoid family has long attracted natural product, biochemical, organic, and medicinal chemists due to continuous discoveries regarding their isolation, characterization, pharmacology, biosynthesis, and chemical synthesis. Over the past decade, our group has conducted numerous studies focusing on the semisynthesis and biological screening of various aromatic abietanes. Their unique tricyclic scaffold and potential for selective chemical functionalization make them attractive building blocks for developing bioactive molecules. The availability of chiral natural (+)-carnosic acid at a low price encouraged us to use it as a starting material.

In this work, we disclose how a simple modification to the carbon skeleton of carnosic acid, specifically the introduction of a formyl group, yields a more potent analogue, methyl 11,12-di-*O*-methyl-14-formylcarnosate, in a panel of solid tumor cell lines. The structural characterization was elucidated by extensive 1H, 13C, and 2D-NMR analysis. Preliminary biological evaluation across several tumor cell lines showed relevant antiproliferative activity. Notably, this formyl derivative demonstrated six-fold greater potency than cisplatin and etoposide in T47D (breast) and WiDr (colon) cells.

Author contributions: Conceptualization, Jose M. Padron and Miguel A. González-Cardenete; Methodology, Nerea Lluch-Cerezo, William E. Mendoza-Hernández, Aday González-Bakker, Jose M. Padron and Miguel A. González-Cardenete; Validation, Aday González-Bakker, Jose M. Padron and Miguel A. González-Cardenete; Formal analysis, William E. Mendoza-Hernández, Aday González-Bakker, Jose M. Padron and Miguel A. González-Cardenete; Investigation, Nerea Lluch-Cerezo, William E. Mendoza-Hernández, Aday González-Bakker, Jose M. Padron and Miguel A. González-Cardenete; Resources, Miguel A. González-Cardenete; Data curation, Nerea Lluch-Cerezo, William E. Mendoza-Hernández, Aday González-Bakker and Jose M. Padron; Writing - original draft, Nerea Lluch-Cerezo; Writing - review and editing, Jose M. Padron and Miguel A. González-Cardenete; Supervision, Jose M. Padron and Miguel A. González-Cardenete; Project administration, Jose M. Padron and Miguel A. González-Cardenete; Funding acquisition, Jose M. Padron and Miguel A. González-Cardenete;



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Sciforum-211341: Anogeissus leiocarpus roots as a promising source of potent antimicrobial and antioxidant agents

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Background: Infections pose an increasing health burden in people living with diabetes, and it worsened by antimicrobial resistance.

Objective: This study assessed the antimicrobial and antioxidant properties of *Anogeissus leiocarpus.*

Materials and methods: Five different bacterial and fungal strains were tested: *Escherichia coli* ATCC 25922, *Klebsiella pneumoniae* ATCC 700603, *Pseudomonas aeruginosa* ATCC 27853, *Staphylococcus aureus* ATCC 29213, and *Candida albicans* ATCC 35659.

The Antimicrobial activity of the hydroethanolic extract of *Anogeissus leiocarpus* roots was determined by agar well diffusion (inhibition zone diameters). The minimum inhibitory concentration (MIC) and minimum microbicidal concentration (MMC) were measured using the broth dilution method. The *in vitro* antioxidant potential was assessed through the hydroxyl radical scavenging, Nitric oxide scavenging, and iron chelating assays.

Results: The hydroethanolic extract of *Anogeissus leiocarpus* roots exhibited broad-spectrum antimicrobial activity with MIC values ranging from 3.91 to 62.5 mg/mL, inhibiting both Gram-positive and Gram-negative bacteria (19.90 - 27.09 mm) and *Candida albicans* (15.59mm). The extract showed bactericidal and fungicidal activities against the five different bacterial and fungal strains, with MBC/MIC and MFC/MIC ratios ≤ 4. *Staphylococcus aureus* strain with the lowest MIC (MIC = 3.91 mg/mL) was the most susceptible among the Gram-positive strains. *In vitro*, it also demonstrated concentration-dependent antioxidant activity by scavenging the NO and OH radicals and chelating Fe ions.

Conclusion: These findings indicate that *Anogeissus leiocarpus* roots could serve as a natural source of antimicrobial and antioxidant agents, potentially useful in managing infections commonly associated with the diabetic population.

Author contributions: Conceptualization, Aku Enam MOTTO; Methodology, Aku Enam MOTTO; Formal analysis, Aku Enam MOTTO; Investigation, Aku Enam MOTTO; Data curation, Aku Enam MOTTO;



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Sciforum-211346: Preclinical Evaluation of UNIM-H and UNIM-R Polyherbal Formulations for the Management of Experimental Arthritis

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Arthritis is a chronic inflammatory disorder characterized by persistent inflammation, joint damage, and dysregulated inflammatory pathways, necessitating safer and effective therapeutic approaches. This study evaluated the safety, chemical profile, and antiarthritic potential of two polyherbal formulations, UNIM-H for oral administration and UNIM-R for topical application. UNIM-H was investigated through acute and 28-day toxicity, cytotoxicity, carrageenan-induced paw oedema, cotton pellet-induced granuloma, and complete Freund's adjuvant (CFA)-induced arthritis models, whereas UNIM-R was assessed for dermal safety, irritation, cytotoxicity, and antiarthritic efficacy. HPTLC profiling confirmed characteristic chemical markers in UNIM-H, including aloe-emodin, colchicine, guggulsterone-Z, and quercetin, while UNIM-R contained 1,8-cineole, benzoic acid, sesamol, and quercetin, supporting chemical standardization of both formulations. UNIM-H demonstrated strong in vitro antioxidant and anti-inflammatory activities, with IC_{50} values of 0.0352 and 2.078 mg/mL, respectively. In vivo, UNIM-H at 200 and 400 mg/kg and the topical UNIM-R formulation produced significant reductions in paw oedema and inflammatory mediators, including TNF-α, IL-1β, IL-02, IFN-γ, and PGE_2, along with modulation of the anti-inflammatory cytokine IL-10. Histopathological and radiographic findings further supported the antiarthritic effects of both formulations, with responses comparable to those observed with the respective reference drugs, indomethacin (3 mg/kg) for UNIM-H and diclofenac gel for UNIM-R. Molecular assessment further demonstrated changes in MMP-9 gene expression and COX-2 and LOX protein expression, indicating modulation of key inflammatory and joint-destructive pathways. Overall, UNIM-H and UNIM-R demonstrated promising complementary oral and topical antiarthritic activity, with favorable safety profiles and defined chemical-marker characteristics, supporting their further preclinical development.

Author contributions: Conceptualization, Ahmad Ali, Nikhat Shaikh and Tabassum Khan; Methodology, Ahmad Ali, Pawan Sharma, Binita Ashok Mandal, Nikhat Shaikh, Tabassum Khan and Falak Bamne; Software, Tabassum Khan; Validation, Ahmad Ali and Nikhat Shaikh; Formal analysis, Pawan Sharma, Binita Ashok Mandal, Tabassum Khan and Falak Bamne; Investigation, Pawan Sharma, Binita Ashok Mandal, Tabassum Khan and Falak Bamne; Resources, Pawan Sharma and Nikhat Shaikh; Data curation, Nikhat Shaikh; Writing - original draft, Pawan Sharma and Falak Bamne; Writing - review and editing, Ahmad Ali, Pawan Sharma, Binita Ashok Mandal, Nikhat Shaikh, Tabassum Khan and Falak Bamne; Visualization, Ahmad Ali and Pawan Sharma; Supervision, Ahmad Ali, Nikhat Shaikh and Tabassum Khan; Project administration, Ahmad Ali; Funding acquisition, Ahmad Ali;

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Sciforum-211357: Solvent-Dependent Phenolic Recovery and Biological Activities of Olive Pomace Extracts

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Olive pomace, a by-product of the olive oil industry, represents an underexploited source of bioactive compounds with potential health applications. Their recovery is influenced by extraction conditions, particularly solvent polarity, which may affect extract composition and biological activity. This study aimed to evaluate the influence of extraction solvent on the phenolic content and biological properties of olive pomace extracts. Extracts were obtained by ultrasound-assisted extraction using methanol, ethanol, ethanol:water (70:30, v/v), and acetone. Extraction yield was determined gravimetrically, while total phenolic content was quantified using the Folin–Ciocalteu method. Antioxidant activity was assessed using the DPPH radical scavenging assay. Antimicrobial activity was evaluated against bacterial and yeast strains through minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) assays. Preliminary toxicity was assessed using the *Artemia salina* lethality model. Solvent selection influenced extraction yield and phenolic recovery. The ethanol:water extract showed the highest extraction yield (10.56%) and total phenolic content (29.53 mg GAE/g extract), followed by methanol (20.92 mg GAE/g extract). Ethanol:water and methanol extracts also exhibited the highest DPPH scavenging activity, reaching approximately 37% inhibition. Antimicrobial activity was comparable among the extracts for most tested microorganisms. For *Enterococcus faecalis*, the acetone extract showed the lowest MIC (78.1 µg/mL), compared with 156.3 µg/mL for methanol and 312.5 µg/mL for the remaining extracts. Overall, these findings demonstrate that solvent selection affects phenolic recovery and antioxidant activity, while antimicrobial activity showed a less pronounced dependence on extraction solvent.

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Author contributions: Conceptualization, Patrícia Rijo; Methodology, Rebeca André and Patrícia Rijo; Validation, Patrícia Rijo; Formal analysis, Rebeca André and Vera M. S. Isca; Investigation, Rebeca André, Inês Saraiva and Vera M. S. Isca; Resources, Patrícia Rijo; Data curation, Patrícia Rijo; Writing - original draft, Rebeca André; Supervision, Rebeca André and Patrícia Rijo; Project administration, Rebeca André and Patrícia Rijo; Funding acquisition, Patrícia Rijo;



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Sciforum-211372: Network pharmacology of cyanidin-3-O-glucoside in oxidative stress-mediated drug-induced liver injury.

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Background: Cyanidin-3-O-glucoside (C3G) is a prominent dietary anthocyanin abundant in dark berries, widely recognized for its potent antioxidant and anti-inflammatory properties. Despite its documented hepatoprotective potential, the comprehensive, systems-level molecular mechanisms by which C3G counteracts oxidative stress-mediated drug-induced liver injury (DILI) remain to be fully characterized.**Objective:** This study aimed to systematically map the network pharmacology of C3G in the context of oxidative stress-induced inflammatory liver injury, with a specific focus on the Nrf2/HO-1/ROS antioxidant enzyme axis.**Methods:** Candidate therapeutic targets of C3G were retrieved from public chemogenomic databases and intersected with disease-associated genes specific to oxidative stress and liver injury. A comprehensive protein–protein interaction (PPI) network was constructed, followed by topological hub gene analysis and GO/KEGG pathway enrichment profiling. To prioritize mechanistically relevant targets, a custom C3G Oxidative Stress Modulation Score was implemented. Structural interactions were further evaluated via molecular docking simulations against the KEAP1 repressor protein.**Results:** The integrated network topology successfully identified *NFE2L2* (Nrf2), *KEAP1*, *HMOX1* (HO-1), *NQO1*, *SOD2*, *CAT*, *GPX1*, *GCLC*, *RELA*, and mitogen-activated protein kinase (MAPK)-related signaling proteins as central functional nodes. These targets directly link C3G exposure to cellular antioxidant defenses and the modulation of redox-sensitive inflammatory stress pathways.**Conclusion:** This study establishes a systems-level pharmacology model demonstrating that cyanidin-3-O-glucoside effectively attenuates oxidative stress-mediated liver injury. This hepatoprotective effect is achieved through the coordinated activation of the Nrf2/HO-1 signaling axis, enhancement of downstream ROS detoxification enzymes, and suppression of inflammatory cascades.



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Sciforum-211389: Polyphenolic Content and In Vitro Anti-Inflammatory Activity of Leaf Fractions from a Bulgarian Fig Cultivar (Ficus carica L.)

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The fig tree (*Ficus carica* L.) is a valuable medicinal and food crop known for its rich content of biologically active compounds. The present study aims to evaluate the total phenolic and flavonoid contents, as well as the *in vitro* anti-inflammatory potential of fractions (n-hexane, chloroform, ethyl acetate, butanol, and aqueous) obtained from the leaves of a Bulgarian fig cultivar. The total phenolic content (TPC) and total flavonoid content (TFC) were determined spectrophotometrically and expressed as mg GAE/g extract and mg QE/g extract, respectively. The anti-inflammatory activity was evaluated using the inhibition of albumin denaturation (IAD) assay and expressed as IC_{50} values (µg/mL). The results demonstrated significant variations among the different fractions. The ethyl acetate fraction (EtOAc) exhibited the highest phenolic (458.79 mg GAE/g) and flavonoid (219.66 mg QE/g) contents, followed by the butanol (BuOH; TPC: 64.70 mg GAE/g; TFC: 40.96 mg QE/g) and aqueous fractions (H_2O; TPC: 59.75 mg GAE/g; TFC: 11.64 mg QE/g). Flavonoids were not detected in the n-hexane (n-H) and chloroform ($CHCl_3$) fractions. In the inhibition of albumin denaturation assay, the lipophilic n-hexane fraction demonstrated the highest anti-inflammatory activity with the lowest IC_{50} value (27.54 µg/mL), followed by the ethyl acetate (30.74 µg/mL), butanol (32.11 µg/mL), and chloroform (37.47 µg/mL) fractions. The aqueous fraction showed no inhibitory activity. In conclusion, extraction with solvents of varying polarity enables the effective fractionation of bioactive compounds from fig leaves. The lipophilic and ethyl acetate fractions possess pronounced anti-inflammatory potential, making the Bulgarian fig cultivar a promising source of natural biologically active substances.



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Sciforum-211395: Phytochemical characterization and evaluation of the antiproliferative activity of *Chelidonium majus* extract in tumor cell models

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Cancer is one of the main challenges of contemporary medicine, determining the need to identify new bioactive molecules with therapeutic potential. In this context, natural plant-derived compounds are an important source for discovering and developing antitumor agents because of their structural diversity and multiple biological activities. *Chelidonium majus* (CM), known as celandine, is a medicinal species rich in bioactive compounds, especially alkaloids, with reported pharmacological effects, including on cellular processes involved in carcinogenesis.

This study aimed to characterize the composition of *Chelidonium majus* extract and evaluate its cytotoxic and antitumor effects in human cell models. We investigated the extract's biological activity using the tumor cell lines HepG-2 (hepatocellular carcinoma) and LoVo (colorectal adenocarcinoma), as well as the non-tumor cell line HUVEC (human endothelial cells). Cisplatin (CisPt) served as the reference agent. Cells were treated with different concentrations of CM extract for 24 and 48 hours, and cell viability was evaluated quantitatively.

CM extract treatment significantly reduced tumor cell viability in a concentration-dependent manner. At 1:8 dilution, cell viability was reduced to approximately 42%, compared to 58% in the case of CisPt, while the effect on HUVEC cells was reduced. These data indicate a differential cytotoxic profile of the CM extract, with a possible selectivity for tumor cells.

Overall, the results demonstrate the biological potential of *Chelidonium majus* extract as a source of compounds with antitumor activity and support further investigation of the cellular and molecular mechanisms involved. Characterizing these mechanisms could help evaluate natural compounds as potential therapeutic agents or adjuvants to conventional antineoplastic treatments.

Author contributions: Conceptualization, Mirela Antonela Mihaila; Methodology, Mirela Antonela Mihaila, Viviana Roman, Mona Luciana Galatanu, CARMEN ELISABETA MANEA and Mariana Popescu; Software, Viviana Roman, Carmen Marinela Mihăilescu and Marinela Bostan; Validation, Mariana Panturoiu and Mariana Popescu; Formal analysis, Mona Luciana Galatanu, Mariana Panturoiu and Marinela Bostan; Data curation, CARMEN ELISABETA MANEA and Carmen Marinela Mihăilescu; Writing - original draft, Mirela Antonela Mihaila; Writing - review and editing, Mirela Antonela Mihaila; Visualization, Carmen Marinela Mihăilescu; Supervision, Marinela Bostan;



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Sciforum-211432: Natural Product-Based Topical Formulation for Burn Wound Healing: A Controlled Study in a Murine Model

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Background: Natural products and multicomponent topical formulations are increasingly investigated for tissue repair, but their efficacy compared with established treatments remains insufficiently characterised. This study evaluated the wound-healing effects of a traditional multicomponent ointment compared with silver sulfadiazine (SSD) in a standardised murine model of second-degree burn injury.

Methods: Standardised second-degree burns were induced in 45 mice using a 1 cm^2 plate heated to 90 °C for 10 s. Animals were randomly allocated to normal saline, SSD, or a traditional topical ointment containing olive oil, lanolin, beeswax, honey, turmeric, salt, henna, egg yolk, and Saqqez (natural gum). The ointment composition was based on a traditional recipe described in the literature, rather than systematic optimisation of ingredient proportions. Treatments were administered daily. Following the loss of six animals, 39 animals were included in the final analysis. Wound area and histopathological parameters, including inflammation, re-epithelialisation, angiogenesis, collagen organisation, and fibroblast proliferation, were evaluated on Days 7 and 14.

Results: Treatment group did not significantly affect wound area overall ($P = 0.740$), whereas wound contraction progressed significantly over time ($P < 0.001$). Both SSD and the traditional ointment showed improved histopathological healing compared with saline. On Day 7, the ointment was associated with greater angiogenesis, more compact collagen fibres, and more pronounced early tissue restoration. By Day 14, SSD showed better collagen organisation, fibroblast proliferation, and tissue maturation. No significant overall morphological differences were observed between the two active-treatment groups.

Conclusions: The traditional multicomponent ointment showed favourable histopathological features of burn wound repair, particularly during the early healing phase, although no significant overall differences were detected between the active treatments. These findings support further investigation of the preparation, including physicochemical characterisation, optimisation of ingredient proportions, and assessment of stability, antimicrobial activity, safety, and clinical applicability.

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Sciforum-211457: Novel methodology for the isolation of soyasaponin as an innovative sialic acid inhibitor with characterisation, and biological evaluation

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Soyasaponin is an oleanane-type triterpenoid characterised by micellar-like properties due to its unique composition of hydrophilic sugar molecules attached to a hydrophobic pentacyclic core. They are classified according to their aglycone type and the number or composition of connected carbohydrate moieties at specified carbon positions. Soyasaponins A and B are defensive molecules that protect plants. These molecules have potent anti-inflammatory, lipid-lowering, and antioxidant properties, making them a target for immunological and metabolic diseases. In the current study, soyasaponin was isolated using thermomechanical and hydrolysis techniques. LC-QToF, NMR, FTIR, and SEM were used to characterise soyasaponin. Cell viability, cellular uptake, wound healing, Annexin V FITC apoptosis, autophagy, and cellular morphology were used to investigate the biocompatibility of soyasaponin against a normal fibroblast cell line. RBC morphology was also used after soyasaponin incubation to assess haemolysis of RBCs. The results confirmed that the isolated soyasaponin has no significant toxicity on normal cells. It also showed significant wound-healing potential in an in vitro study. It can be concluded that isolated soyasaponin can be used as a biodegradable material for biomedical applications and could be transferred to the pharmaceutical industry.

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Sciforum-211467: Formulation and characterization of a natural facial mask incorporating *musa spp.* Peel, *citrullus lanatus* rind, and *centella asiatica* aqueous extracts

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Background: Consumers increasingly demand eco-friendly skincare products. Agricultural waste-based cosmetic formulations offer a sustainable approach to reducing environmental impact while providing skincare benefits. Plant materials such as *Musa spp*. peel (banana peel), *Citrullus lanatus* rind (watermelon rind), and *Centella asiatica* (Indian pennywort) contain flavonoids and phenolic compounds promoting antioxidant activity. These characteristics suggest their potential application in facial mask formulations as natural alternatives to synthetic ingredients. **Objective:** This study aimed to formulate and characterize a natural facial mask incorporating aqueous extracts of *Musa spp.* peel, *Citrullus lanatus* rind, and *Centella asiatica*, and to evaluate its free radical scavenging activity (RSA). **Methods:** Phytochemical tests were performed on the extracts to confirm the presence of flavonoids and phenolic compounds, while antioxidant activity was evaluated using the DPPH assay. The base formulation was selected through pH testing, and the optimal extract formulation was determined through preliminary evaluations. **Results:** All extracts tested positive for flavonoids and phenolic compounds. Banana peel extract at concentrations $>$100 mg/mL showed the highest RSA value, while watermelon rind and Indian pennywort extracts showed their highest RSA values at $>$10 mg/mL. The best base formulation consisted of 20% collagen peptides in pullulan and showed minimal pH variation over three consecutive days. The optimal extract formulation consisting of banana peel, watermelon rind and Indian pennywort extracts in a 10:1:1 ratio, demonstrated the highest RSA value and better moisturizing performance than the other formulations. **Conclusion:** The selected formulation demonstrated high antioxidant and moisturizing properties, highlighting its potential as an effective natural facial mask. By utilizing natural ingredients such as banana peel, watermelon rind, and Indian pennywort, which are rich in flavonoids and phenolic compounds, this formulation offers a sustainable and environmentally friendly skincare alternative.

Author contributions: Conceptualization, Sylvia Sandanamsamy; Methodology, Sylvia Sandanamsamy and Nur Aisyah Naurah Mohamad Fauzi; Validation, Nur Aisyah Naurah Mohamad Fauzi; Formal analysis, Nur Aisyah Naurah Mohamad Fauzi; Investigation, Nur Aisyah Naurah Mohamad Fauzi; Data curation, Nur Aisyah Naurah Mohamad Fauzi; Writing - original draft, Nur Aisyah Naurah Mohamad Fauzi; Writing - review and editing, Nur Aisyah Naurah Mohamad Fauzi; Visualization, Sylvia Sandanamsamy; Supervision, Sylvia Sandanamsamy; Project administration, Sylvia Sandanamsamy;



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Sciforum-211470: Bee Podmore Extract Modulates Osteogenic Differentiation of Metabolically Impaired Mesenchymal Stromal Cells

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Equine metabolic syndrome (EMS) is a naturally occurring endocrine-metabolic disorder that compromises the survival, redox balance, and regenerative competence of adipose-derived mesenchymal stromal cells (EqASCs), limiting their value for autologous cell-based therapy. This study examined whether a hydroethanolic extract of Bee Podmore (BP), the chemically heterogeneous biomass of deceased *Apis mellifera* workers, could restore the osteogenic potential of EMS-derived EqASCs *in vitro*. The extract was characterized at the compound-class level (total phenolic content 45.4 µg GAE/mg, total flavonoid content 5.7 µg QE/mg, BCA-reactive protein equivalent 460 µg/mg, total lipid equivalent 470.3 µg cholesterol-equivalent/mg). Cytocompatibility screening in healthy control and EMS-derived EqASCs identified 60 µg/mL as a conservative, non-cytotoxic working concentration, which was applied to EMS-derived cells during osteogenic induction. Relative to untreated EMS cells, BP treatment restored alkaline phosphatase activity and increased Alizarin Red S-detectable mineralization. This functional recovery was accompanied by reactivation of a coordinated osteogenic gene-expression and protein-distribution program, with upregulation of RUNX2, BMP4, COL1A1, BGLAP, and SPP1 relative to untreated EMS cells. Together, these findings indicate that Bee Podmore, a multi-component apiary by-product, can partially reverse the osteogenic impairment characteristic of EMS-derived EqASCs, supporting its potential as a bioactive supplement to improve the regenerative competence of metabolically compromised stromal cells for future autologous cell-based therapeutic applications in horses.



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Sciforum-211543: A Natural HSV-1 Replication Inhibitor Based on *Tagetes patula* Extract

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The relevance of this study stems from the increasing resistance of herpes simplex virus type 1 (HSV-1) to traditional antiviral drugs and the need to identify novel plant-derived bioactive compounds inhibiting viral replication without promoting resistance. Plants of the genus *Tagetes* are known for a high content of terpenes, flavonoids, and other metabolites that may exhibit antiviral activity; therefore, their investigation provides a promising basis for the development of new plant-based therapeutics.

The aim of this study was to evaluate the effect of a *Tagetes patula* inflorescence ethanol extract on HSV-1 replication post-viral adsorption. Plant material was washed, dried at 25°C, ground (2 g), homogenized in a mortar, and extracted in 20 mL of 70% ethanol (72 h, cool dark place, periodic stirring). The extract was filtered and stored at 4–6°C in the dark until use. Following viral adsorption (1–1.5 h, 37°C, 5% CO_2), culture medium containing extract dilutions (1:400 to 1:50) was added to the cells. Untreated infected Vero cells served as the control. Quantitative assessment of viral DNA was performed by qPCR using a standard curve.

The infectivity titration results demonstrated that the extract exerted a pronounced antiviral effect at dilutions of 1:50–1:200, reducing the HSV-1 titer by 4.49–2.9 $\log_{10}$ $TCID_{50}$/mL. qPCR data confirmed a reduction in viral load across all tested dilutions, with the lowest level of viral DNA observed at the 1:50 dilution, consistent with a marked decrease in cytopathic effect (CPE). The highest viral DNA level was detected at 1:400 extract dilution. Parallel analysis of samples from wells with and without CPE revealed a clear correlation: wells lacking CPE showed significantly higher Ct values, indicating effective inhibition of viral replication.

Overall, the results demonstrate the antiviral activity of the *T. patula* extract and highlight its potential as a source of natural compounds for the development of new treatments against HSV-1.



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Sciforum-211612: Structural Features of Grayanotoxins II and III and Their Affinity for Human Carbonic Anhydrase I: A Molecular Docking Study

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Grayanotoxins are tetracyclic diterpenoid compounds of plants of the family *Ericaceae*, including the genus *Rhododendron.* Grayanotoxins are traditionally believed to target voltage-gated sodium channels, but an extract of honey containing *Rhododendron ponticum* pollen was recently shown to inhibit metal-dependent carbonic anhydrase, an effect attributed to grayanotoxin III (GRTIII). Since such honey may contain other grayanotoxin forms as well, a comparative study of their binding to human carbonic anhydrase is of interest. The aim of this work was to perform molecular docking of grayanotoxin II (GRTII) and grayanotoxin III (GRTIII) into the active site of human carbonic anhydrase I (hCA I) and to identify differences in their binding mechanisms as forms with different toxicity. The geometries of GRTII and GRTIII were optimized in Gaussian 9.0 with reference to X-ray diffraction data (GRTIICCDC:1170390, GRTIIICCDC:1246563); docking was carried out using the CB-DOCK2 method against the hCA I structure (RCSBPDB2FW4). Structurally, GRTII and GRTIII differ in the environment of the tenth carbon atom of the framework: in GRTIII it bears a hydroxyl group and a methyl radical, whereas in GRTII it is involved in an exocyclic double bond with a methylene fragment. According to the docking results, these groups at C10 of the seven-membered ring of GRTIII provide additional binding to hCA I: the methyl radical interacts with tyrosine (Tyr7), and the hydroxyl group interacts with serine (Ser231) and histidine (His64). For GRTII, no binding through this fragment is observed. The stronger binding of GRTIII to the active sites of hCA I was shown to be due to the presence of a hydroxyl group and a methyl radical in the seven-membered ring of the toxin; the results are consistent with published data on the relative toxicity of GRTII and GRTIII.

Author contributions: Conceptualization, Ekaterina Alexandrovna Popova; Methodology, Konstantin Andreevich Sukhomlin ; Investigation, Konstantin Andreevich Sukhomlin ; Writing - original draft, Konstantin Andreevich Sukhomlin ; Writing - review and editing, Ekaterina Alexandrovna Popova; Supervision, Ekaterina Alexandrovna Popova;



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Sciforum-211725: Prioritising Flavonoids Reported in Moroccan Honeys against Influenza A Neuraminidase Structures using Docking Scores and Ligand Efficiency.

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Flavonoids found in honey have been studied for their potential antiviral activity. However, assessing these compounds against a single protein structure does not account for structural variability between targets. Also, it does not show if the compound rankings are consistent across the structures. This study compared the binding profiles of flavonoids reported in Moroccan honeys across multiple influenza A N1 and N2 neuraminidase structures. These flavonoids were studied as candidate complementary antivirals rather than replacements for existing neuraminidase inhibitors.

Molecular docking of 31 flavonoids was performed against ten protein structures: three experimentally determined N1 structures, five experimentally determined N2 structures, and N1 and N2 models based on Moroccan influenza sequences. Oseltamivir, zanamivir and sialic acid were included as reference ligands. Compounds were prioritised primarily using docking scores (LeadFinder LF dG) and ligand efficiency (LF LE). Their physicochemical drug-likeness descriptors were also evaluated.

Catechin gallate and epicatechin gallate ranked first or second on nine out of ten structures, with the most favourable docking score reaching -11.96 kcal/mol. Across the structures, reference ligands scored -6.9 to -9.7 kcal/mol (oseltamivir) and -8.7 to -11.7 kcal/mol (zanamivir). Both gallates received more favourable docking scores than oseltamivir on every structure and scores equal to or more favourable than zanamivir on most. Compound rankings showed strong agreement across the structures, including the Moroccan models (Kendall's W = 0.79, $p < 10^{-30}$). Gallocatechin ranked third on every structure but had the most favourable ligand efficiency in the series (-0.42 kcal/mol per heavy atom, comparable to zanamivir under the same protocol), with a molecular weight of 306 Da.

These results support selecting gallocatechin and the gallated catechins for molecular dynamics simulations and experimental testing. The docking-score rankings were not dependent on any single protein structure. These predictions do not establish neuraminidase inhibition or antiviral activity.

Author contributions: Conceptualization, Lavinia Dorothea Frau-Vaughn Joseph; Methodology, Lavinia Dorothea Frau-Vaughn Joseph; Software, Lavinia Dorothea Frau-Vaughn Joseph; Investigation, Lavinia Dorothea Frau-Vaughn Joseph; Data curation, Lavinia Dorothea Frau-Vaughn Joseph; Writing - original draft, Lavinia Dorothea Frau-Vaughn Joseph; Writing - review and editing, Lavinia Dorothea Frau-Vaughn Joseph; Visualization, Lavinia Dorothea Frau-Vaughn Joseph; Supervision, Hicham Oumzil;



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Sciforum-211739: Unlocking the Antioxidant Potential of Wild Bilberry (Vaccinium myrtillus L.) Pomace through Design of Experiments

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The valorization of plant-derived waste through bioconversion and biorefinery strategies is gaining increasing attention as a suitable approach to resource recovery. These residues represent a valuable source of bioactive compounds, offering the dual benefit of reducing waste generation while obtaining potentially health-promoting ingredients.

Within this framework, this study aimed to characterize the chemical profile and antioxidant potential of wild bilberry-derived (*Vaccinium myrtillus* L.) pomace. A mathematical and statistical approach based on the Box-Behnken design of experiments was used to optimize the extraction process. Thirteen maceration experiments were designed to extract polyphenolic components from *V. myrtillus* pomace. The total phenolic and flavonoid contents of extracts were determined by the Folin–Ciocalteu assay and aluminum chloride colorimetric assay, respectively.

Non-cell-based radical scavenging assays, i.e., DPPH and ABTS, and the ferric reducing antioxidant power (FRAP) assay were performed to evaluate the antioxidant potential. In addition, cytocompatibility and antioxidant assays were carried out to investigate the antioxidant activity of the extracts in HaCaT cells.

The results showed that all the extracts of *V. myrtillus* were rich of phenolic and flavonoids, and exhibited high radical scavenging and reducing power effects. Selected tested extracts at their lower concentration showed antioxidant potential in HaCaT cells with no signs of toxicity. Taking these results together, the most promising extracts will be considered for the development of a topical product aimed at supporting microcirculatory well-being.

In conclusion, this ongoing research offers valuable data to support the use of *V. myrtillus* pomace extracts for therapeutic purposes.

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Sciforum-211900: Effects of fisetin on peroxynitrite concentration and amyloid content in the hypothalamus and cerebral cortex of rats with type 2 diabetes

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Background: Diabetes is associated with neuronal oxidative and nitrosative stress and may alter amyloid-associated processes. Fisetin is a bioactive flavonoid with antioxidant and neuroprotective properties. This study evaluated the effects of fisetin on peroxynitrite concentration and amyloid fluorescence in the hypothalamus and cerebral cortex of control and diabetic rats.

Methods: Forty rats were assigned to four groups according to diabetes status (control or diabetic) and fisetin treatment (-/+), with 10 animals per group. Type 2 diabetes was induced by feeding rats a high-fat diet for 12 weeks and administering a single intraperitoneal dose of streptozotocin (35 mg/kg). During the subsequent 8 weeks, fisetin-treated animals received fisetin at 20 mg/kg/day by oral gavage. Peroxynitrite concentration and amyloid fluorescence were assessed in the hypothalamus and cerebral cortex. Effects of brain region, fisetin treatment, diabetes status, and their interactions were analyzed using three-way analysis of variance.

Results: Peroxynitrite concentration showed a significant brain-region effect ($p < 0.0001$) and a significant diabetes × fisetin interaction ($p=0.0070$), whereas the main effects of diabetes ($p=0.4422$) and fisetin ($p=0.4889$) were not significant. Amyloid content differed significantly between brain regions ($p=0.0001$) and showed a significant brain region × diabetes interaction ($p=0.0379$). Neither the main effect of fisetin ($p=0.2685$) nor interactions involving fisetin were significant for amyloid fluorescence.

Conclusions: The effect of fisetin on cerebral peroxynitrite concentration depended on diabetes status rather than representing a uniform treatment effect. In contrast, amyloid content was primarily associated with brain region and its interaction with diabetes. These findings indicate distinct region- and disease-context-dependent responses of neuronal nitrosative and amyloid-associated processes to fisetin treatment.

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Sciforum-212092: Deciphering the Antioxidant, Hemocompatibility, and Antimicrobial Properties of *Artemisia arborescens* Essential Oil

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Introduction: *Artemisia arborescens L.* is an aromatic Mediterranean plant used in traditional folk medicine and valued as a source of biologically active volatile constituents (1,2). This study evaluated the antioxidant, hemocompatibility, and antimicrobial properties of its essential oil (AAEO).

Materials and Methods: DPPH• and ABTS•+ assays were used to quantify the antioxidant capacity. Hemocompatibility was assessed by incubating human erythrocytes with AAEO (25-400 µg/mL) for 30 minutes at 37°C, then measuring the percentage of hemoglobin release spectrophotometrically. Antibacterial and antifungal activity were evaluated via broth microdilution and resazurin viability assays, and the minimum bactericidal and fungicidal concentrations were determined by subculturing aliquots from wells displaying no microbial growth.

Results and Discussion: AAEO exhibited antioxidant activity, with IC_{50} values of 164.44 ± 7.10 µg/mL and 116.40 ± 2.78 µg/mL in the DPPH• and ABTS•+ assays, respectively. At 25, 50, and 100 µg/mL, hemolysis did not reach 5%, which is the standard mean hemolytic threshold above which a substance is considered hemolytic. At 200 and 400 µg/mL, hemolysis increased to 9.8% and 13.0%, suggesting a concentration-dependent hemolytic effect at higher concentrations. Hemolysis at all tested concentrations remained significantly lower than that of the positive control ($p < 0.0001$). AAEO inhibited *Staphylococcus aureus* with an MIC and MBC of 2% (v/v), whereas those values for *Enterococcus faecalis*, *Escherichia coli*, and *Klebsiella pneumoniae* were >2% (v/v). Antifungal activity was observed against *Penicillium cyclopium* and *Candida albicans*, with MIC values of 1% and 2% (v/v), respectively. MFC values were >2% (v/v) for both fungi, indicating no fungicidal activity within the tested concentration range. Overall, AAEO demonstrated antioxidant activity, favorable erythrocyte compatibility at concentrations up to 100 µg/mL, while higher concentrations produced a measurable hemolytic response and selective antimicrobial effects.

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Sciforum-212194: Grape antioxidant dietary fibre regulates intrinsic/extrinsic caspase activity balance and epithelial homeostasis in the colon

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Background and Aim: Grape antioxidant dietary fibre (GADF) is a bioactive compound obtained from grape by-products, containing dietary fibre and polyphenols with antioxidant and biological activities. Previous studies have shown beneficial effects of GADF on intestinal health, including modulation of oxidative status, epithelial turnover and barrier function. As apoptosis is essential for epithelial renewal but excessive activation may impair epithelial integrity, this study aimed to investigate the effect of GADF supplementation on the balance between intrinsic and extrinsic apoptotic pathways and its association with epithelial apoptosis and mucosal integrity.

Methods: Animals were supplemented with GADF for 4 weeks. Proximal colon samples were collected for histological and molecular analyses. Apoptosis was evaluated by TUNEL staining, while mucosal architecture was assessed by H&E and PAS staining. Caspase-9 and caspase-8 activities were analysed, and the intrinsic/extrinsic apoptotic balance was calculated as ln(caspase-9/caspase-8). Statistical analyses included unpaired two-tailed Student's t-test or Mann–Whitney U test, as appropriate. Pearson's correlation coefficient was used for parametric correlations.

Results: GADF markedly reduced the intrinsic/extrinsic caspase activity balance, decreasing the caspase-9/caspase-8 ratio by 80.6% ($p < 0.001$), indicating a lower relative contribution of intrinsic apoptotic signalling. This shift was accompanied by a 56.4% reduction in TUNEL-positive cells ($p < 0.01$) and increased PAS staining (+21.9%, $p < 0.01$), suggesting improved mucosal functional features. Mucosal thickness decreased by 14.4% ($p < 0.001$). Caspase activity balance correlated with epithelial apoptosis and mucosal functional parameters, but not with mucosal thickness.

Conclusions: GADF preferentially modulates intrinsic apoptotic signalling by reducing the caspase-9/caspase-8 activity balance. This apoptotic reprogramming is associated with reduced epithelial apoptosis and preservation of mucosal functional features, supporting coordinated regulation of cell death and intestinal homeostasis

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Sciforum-212423: Unlocking the Potential of Bee-Derived Bioactives: From Composition to Optimized Encapsulation

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Royal jelly and propolis are bee-derived natural products containing bioactive compounds with potential applications in pharmaceutical and nutraceutical formulations. In the BEE-TECH project, propolis, and royal jelly will first be characterized in terms of moisture, ash, total protein, and fat contents to obtain information on their composition. Moisture will be determined using the vacuum drying method, while ash, protein, and fat contents will be evaluated according to AOAC 920.153, AOAC 960.52, and AOAC 991.36, respectively. This compositional information, together with information reported in the literature, will be used to guide the selection of suitable encapsulation techniques and conditions for royal jelly and propolis. Different encapsulation techniques, including spray drying, fluid-bed drying, freeze drying, and liposome-based encapsulation, will be investigated for the protection and stabilization of their bioactive compounds. Spray drying will be mainly evaluated due to its flexibility, relatively low cost, and ability to produce stable particles. Natural polysaccharides, including gum arabic and maltodextrin, will be used as wall materials, individually and in combination, at different concentrations. Feed temperature, feed flow rate, and core-to-wall material ratio will be studied and optimized. In addition, liposomal encapsulation using lecithin and chitosan will be investigated. The resulting formulations will be evaluated in terms of encapsulation efficiency and structural uniformity. The combined compositional, literature, and formulation data will support the development of optimized encapsulation protocols for royal jelly and propolis, focusing on stable and uniform structures with high encapsulation efficiency.

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Sciforum-212656: Luteolin–gadolinium complex attenuates inflammatory responses and modulates STAT3–NLRP3 signaling in compound 48/80-stimulated HMC-1 cells

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Mast cell activation and inflammatory mediator release are central to the pathogenesis of urticaria. Luteolin has anti-inflammatory and anti-allergic properties; however, the effects and underlying mechanisms of the luteolin–gadolinium rare-earth complex (LutGdRCS) in mast cells remain unclear. This study investigated the effects of LutGdRCS on inflammatory responses and STAT3–NLRP3 signaling in Compound 48/80-stimulated HMC-1 cells. Cell viability and membrane integrity were assessed using Cell Counting Kit-8 and lactate dehydrogenase (LDH) release assays, respectively. Histamine, interleukin (IL)-1β, IL-6, and tumor necrosis factor (TNF)-α concentrations in culture supernatants were quantified by enzyme-linked immunosorbent assay, and proteins associated with STAT3–NLRP3 signaling were assessed by Western blotting. At the concentrations used for subsequent experiments, Compound 48/80 (10 μg/mL), luteolin (2.5 μg/mL), and LutGdRCS (10 μg/mL) did not significantly reduce cell viability or increase LDH release. Compound 48/80 significantly increased histamine, IL-1β, IL-6, and TNF-α concentrations in culture supernatants, whereas luteolin and LutGdRCS significantly attenuated these increases ($P < 0.05$). Western blotting further showed that LutGdRCS reduced p-STAT3, NLRP3, caspase-1 p20, and IL-1β p17 protein levels in stimulated cells. These findings indicate that LutGdRCS attenuates inflammatory mediator responses in HMC-1 cells and that these effects are associated with reduced p-STAT3 levels and NLRP3 inflammasome signaling, supporting further investigation of LutGdRCS in experimental mast cell-mediated inflammation.

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Author contributions: Conceptualization, SURUI A, Dugarmaa Ulzii and Jihai Shi; Methodology, SURUI A; Validation, Enkhtur Yadamsuren; Formal analysis, SURUI A; Investigation, SURUI A; Data curation, SURUI A; Writing - original draft, SURUI A; Writing - review and editing, Enkhtur Yadamsuren, Dugarmaa Ulzii and Jihai Shi; Visualization, SURUI A; Supervision, Dugarmaa Ulzii and Jihai Shi; Project administration, Jihai Shi; Funding acquisition, Jihai Shi;



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Sciforum-212747: From Traditional Plants to Functional Innovation: Development and Functional Characterization of a Nettle–Fenugreek–Lemon Peel Herbal Tea: Phytochemical, Antioxidant, Anti-Inflammatory, and Mineral Properties

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Abstract

The development of plant-based functional formulations has gained increasing interest as an approach to valorizing natural resources and exploring their potential health-related applications. This study aimed to develop and characterize a herbal tea formulation combining *Urtica dioica* (nettle), *Trigonella foenum-graecum* (fenugreek), and lemon peel. These plant materials have been reported to contain several bioactive constituents, including phenolic acids and flavonoids in *U. dioica*, trigonelline, diosgenin, and steroidal saponins in *T. foenum-graecum*, as well as flavanones and other phenolic compounds in lemon peel.

The formulation was evaluated for its phytochemical, antioxidant, anti-inflammatory, and mineral characteristics. Total polyphenols, flavonoids, and tannins were quantified using spectrophotometric methods. Antioxidant activity was assessed using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical-scavenging assay and reducing power, while anti-inflammatory activity was evaluated through inhibition of protein denaturation. Mineral analysis included the determination of iron, zinc, and magnesium, together with selected potentially toxic metals.

The formulation showed total polyphenol, flavonoid, and tannin contents of 96.5 ± 2.1 mg GAE/g, 45.8 ± 1.6 mg QE/g, and 32.4 ± 1.2 mg CE/g, respectively. It exhibited substantial antioxidant activity, with 81.4% DPPH radical-scavenging activity and an IC_{50} value of 245.7 µg/mL, together with a reducing power of 1.92 ± 0.08 mmol Fe^{2+}/g. The formulation also demonstrated anti-inflammatory activity, reaching 72.3% inhibition of protein denaturation at the highest tested concentration ($p < 0.01$). Mineral analysis revealed iron, zinc, and magnesium concentrations of 8.72 ± 0.14 mg/L, 3.45 ± 0.10 mg/L, and 12.9 ± 0.18 mg/L, respectively. The levels of the investigated potentially toxic metals, including lead, cadmium, and aluminum, remained within the safety limits considered in this study.

Overall, the developed herbal tea exhibited a phytochemically rich composition, marked antioxidant and *in vitro* anti-inflammatory activities, and a favorable mineral profile. However, individual phytochemical constituents were not experimentally identified in the present study. Further investigations using chromatographic techniques such as HPLC or LC-MS are therefore required to identify and quantify the specific bioactive compounds present in the formulation and to further evaluate their bioavailability, safety, and biological effects.



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Sciforum-212987: Potential protective effects of epicatechin against oxidative stress in experimental diabetes

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Diabetes mellitus is associated with increased oxidative stress and disturbances in hepatic metabolism, which may contribute to hepatocellular dysfunction. Epicatechin, a naturally occurring flavonoid, has demonstrated antioxidant and metabolic regulatory properties in previous experimental studies. The present study aimed to investigate the potential protective effects of epicatechin against oxidative stress and biochemical alterations in the liver of rats with experimental diabetes. White Wistar rats were used to establish an experimental diabetes model, followed by epicatechin administration. The effects of treatment were evaluated using biochemical and oxidative stress-related parameters, including malondialdehyde (MDA), superoxide dismutase (SOD), reduced glutathione (GSH), lactate dehydrogenase (LDH), alanine aminotransferase (ALT), and aspartate aminotransferase (AST). Blood glucose levels and selected hepatic biochemical parameters were also assessed to characterize metabolic alterations. Epicatechin administration was associated with attenuation of oxidative stress, reflected by improved SOD and GSH status and reduced MDA levels. Improvements in hepatic marker enzymes, including ALT, AST, and LDH, as well as blood glucose levels, were also observed compared with the diabetic control group. These findings suggest that epicatechin may exert a protective effect against diabetes-associated hepatic dysfunction, potentially through attenuation of oxidative stress and improvement of metabolic homeostasis. The findings provide a basis for further investigations, including complementary in vitro studies, to clarify the cellular effects and mechanisms underlying the observed protective activity of epicatechin.



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Sciforum-213031: A Metabolomics-Based Investigation of Neem's Therapeutic Effect on Breast Cancer

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Ethanolic Neem (*Azadirachta indica*) leaf extract (ENLE) has shown antiproliferative and pro-apoptotic effects in breast cancer cells, but its metabolic effects remain poorly uncharacterized. Previous research has investigated the chemical and biological profiles of *Azadirachta indica* [1]. This study characterized the extracellular metabolic response to ENLE treatment in two molecularly distinct breast cancer cell lines and compared these responses with doxorubicin.

ENLE was prepared by ethanolic maceration of botanically authenticated *Azadirachta indica* leaves. Cytotoxicity was assessed by the sulforhodamine B assay after 72 h in MCF-7 (estrogen receptor-positive) and MDA-MB-231 (triple-negative) cells. Conditioned media from 72-h treatments (n = 3 per group) with i) ENLE at experimentally determined IC_{30} concentrations, ii) doxorubicin at literature-derived IC_{30} concentrations, and iii) matched DMSO vehicle, were subjected to untargeted LC-MS metabolomic analyses, followed by multivariate, differential and quantitative enrichment analyses using MetaboAnalyst 6.0.

ENLE reduced viability in a concentration-dependent manner, with MCF-7 cells being more sensitive than MDA-MB-231 (IC_{50} 29.99 versus 42.28 µg/mL, respectively). ENLE significantly altered 49 out of 107 putatively annotated compounds in MCF-7 cells, and 58 out of 118 in MDA-MB-231 cells. Treatment groups showed distinct separation by PCA and PLS-DA in both cell lines, with permutation testing supporting supervised separation. Long-chain acylcarnitines, LysoPE(18:1), kynurenine and hypoxanthine exhibited cell-line-dependent directional changes, whereas LysoPC(20:4) and 9(10)-EpODE increased and nicotinate D-ribonucleoside decreased in both without being reproduced by doxorubicin. Eighteen ENLE-associated changes in MCF-7 and 33 in MDA-MB-231 were shared with doxorubicin, while direct comparison identified respective 39 and 35 significant differences.

In conclusion, ENLE exerted cytotoxic activity and induced a cell-line-dependent extracellular metabolic response that partially overlapped with, yet remained distinguishable from, doxorubicin. These extracellular metabolic changes highlight candidate metabolic pathways and processes for further mechanistic investigation and characterization.

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Sciforum-214009: From resveratrol to trimethoxystilbene: HPLC and docking reveal enhanced inhibition of PDE1 and PDE4

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Phosphodiesterases (PDEs) control cyclic nucleotide signaling and are established targets in inflammatory disease, with PDE1 and PDE4 being especially relevant for the regulation of cAMP. Here, we asked whether methylating the hydroxyl groups of resveratrol (RSV), which yields 3,4,5′-trimethoxy-trans-stilbene (TMS), improves its ability to inhibit these two isoenzymes.

Using an optimized HPLC assay that follows cAMP hydrolysis, we determined the kinetic and inhibition parameters of both enzymes. PDE4 showed a higher substrate affinity than PDE1. RSV proved to be a weak inhibitor, whereas TMS was approximately 4-fold (PDE1) and 8-fold (PDE4) more potent. The reference inhibitor roflumilast remained clearly superior, acting in the nanomolar range.

Molecular docking placed RSV, TMS and roflumilast in the same catalytic pocket, in contact with conserved residues such as glutamine. The higher potency of TMS can be explained by its better fit within the hydrophobic active site, which strengthens ligand–enzyme interactions.

These results show that trimethylation boosts the PDE-inhibitory capacity of resveratrol derivatives and point to TMS as a dual PDE1/PDE4 modulator, illustrating the value of combining experimental and computational approaches.

Author contributions: Conceptualization, Adrián Matencio and José Manuel López-Nicolás; Investigation, Antonio Sanchez Belmonte; Supervision, Adrián Matencio and José Manuel López-Nicolás;



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Session 5. Novel Methodologies and AI

Sciforum-207719: A Hybrid Computational Framework for Gastroretentive Drug Delivery: Integrating PBPK Modelling and Design of Experiments for Systematic Formulation Optimisation

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Introduction: In resource-limited settings, extensive experimental formulation screening is impractical. Cimetidine, an H_2-receptor antagonist, suffers from low oral bioavailability (30–40%) and a short half-life, demanding gastroretentive delivery. We hypothesised that a hybrid framework integrating Physiologically Based Pharmacokinetic (PBPK) modelling with Design of Experiments–Response Surface Methodology (DoE-RSM) could efficiently optimise an in-situ gelling system, providing a cost-effective alternative to extensive pharmacokinetic studies.**Methods:** PBPK modelling (PK-Sim® v11.3), using a proxy population with parameter adjustments representative of Sub-Saharan African physiology, predicted how the pH-responsive buoyant system modulates cimetidine absorption, including gastric residence time and viscosity targets. A 10-run Central Composite Design then optimised sodium alginate (2–6% w/v) and calcium carbonate (0.5–1.5% w/v), targeting buoyancy lag time ($<$5 min), floating duration ($>$8 h) and pH compatibility. Model performance was assessed via R^2, F-statistics and residual diagnostics.**Results:** PBPK predicted a mean residence time of 32.08 h and AUC_inf of 27,106 µmol.min/L (comparative validation pending). DoE-RSM identified sodium alginate as the dominant factor (buoyancy lag coefficient +1.16, $p=3.29\times10^{-5}$, $R^2=0.813$). The model-optimised formulation (4% alginate, 1% $CaCO_3$) predicted a buoyancy lag time of 4.71 min and viscosity of 555.4 cP; experimental confirmation is required. R^2 ranged from 0.65 to 0.813 ($p<0.01$).**Conclusions:** This proof-of-concept computational framework demonstrates the feasibility of combining mechanistic PBPK prediction with statistical DoE-RSM for gastroretentive formulation development. The PBPK approach, using a proxy African population and parameter adjustments, offers a cost-effective alternative to extensive PK studies, is valuable in resource-limited settings, and provides a methodology applicable to other acid-labile drugs with narrow absorption windows. Key limitations include unvalidated predictions, the limited 10-run design, and the absence of experimental and in vivo corroboration.

Author contributions: Conceptualization, VANESSA DANAI BEREJENA and Humphrey Masimba Makumbirofa; Formal analysis, VANESSA DANAI BEREJENA; Investigation, VANESSA DANAI BEREJENA; Data curation, VANESSA DANAI BEREJENA; Writing - original draft, VANESSA DANAI BEREJENA; Writing - review and editing, Humphrey Masimba Makumbirofa; Supervision, Humphrey Masimba Makumbirofa;



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Sciforum-209488: Interpretable Machine Learning for Early-Stage Aqueous Solubility Prediction in Drug Discovery Using Molecular Descriptors and Applicability Domain Analysis

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Aqueous solubility is a critical pharmacokinetic parameter that dictates drug formulation, absorption, and oral bioavailability. Because experimental measurement bottlenecks early-stage drug discovery, rapid and reliable computational methodologies are essential for candidate prioritization. This study presents an interpretable artificial intelligence framework for predicting aqueous solubility utilizing the Delaney ESOL dataset (1,128 organic compounds). We engineered models using six fundamental structural descriptors: molecular weight, polar surface area, number of rings, rotatable bonds, hydrogen-bond donors, and minimum degree. Five machine learning algorithms were benchmarked: Linear Regression, Decision Trees, Random Forests, Gradient Boosting, and Support Vector Regression.

Non-linear ensemble methods significantly outperformed traditional linear approaches. Random Forest achieved the highest predictive accuracy (RMSE = 0.6748, MAE = 0.4879, R2 = 0.9037). Crucially, feature importance analysis revealed that baseline ESOL-predicted log solubility acts as the dominant feature, allowing the algorithm to function as an advanced recalibration model alongside insights from polar surface area and molecular weight. To ensure reliability for medicinal chemistry applications, an applicability domain (AD) analysis confirmed that 94.7% of test compounds resided within a trustworthy prediction space.

Furthermore, the framework integrates Principal Component Analysis (PCA) and K-means clustering to map chemical spaces, while a Support Vector Classifier (SVC) achieved 85.4% accuracy for binary solubility categorization. This multifaceted workflow transforms solubility prediction from a "black-box" algorithm into a transparent, practical AI methodology, enabling robust virtual screening and faster prioritization of promising pharmacophores.

Author contributions: Conceptualization, Ratikorn Sornumpol;



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Sciforum-210309: Reliable Mutagenicity Triage for Early Medicinal Chemistry: Scaffold-Aware Validation of AI Safety Models

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Early medicinal chemistry requires rapid and dependable identification of potential genotoxic liabilities so that synthetic and experimental resources can be directed toward candidates with more favorable safety profiles. Machine-learning models can support this triage, but their practical value depends on whether reported performance extends to structurally novel chemotypes. Random train–test splitting may give overly optimistic estimates when related compounds occur across partitions, potentially affecting decisions about which chemical series should advance to experimental testing.We evaluated this issue using a curated Ames dataset of 5,362 compounds. Five predictive models were assessed under stratified random splitting and a size- and class-matched Bemis–Murcko scaffold-aware partition designed to increase structural separation while preserving partition size and class proportions. Four models used ECFP4 fingerprints (logistic regression, random forest, XGBoost, and multilayer perceptron), and a simple graph convolutional network was included as a graph-based baseline. Conventional greedy scaffold splitting was additionally examined as a sensitivity analysis.Under matched scaffold-aware evaluation, mean maximum test-to-training ECFP4 Tanimoto similarity decreased from 0.599 to 0.495, while ROC-AUC decreased by approximately 0.04–0.07 across the fingerprint-based models. XGBoost declined from 0.887 to 0.847 and the multilayer perceptron from 0.859 to 0.787. The simple GCN decreased from 0.761 to 0.741. Conventional greedy scaffold splitting produced greater chemical separation, with mean maximum similarity decreasing further to 0.402.These findings indicate that validation design can materially influence the apparent reliability of AI-based mutagenicity screening. By controlling partition size and class balance while challenging models with structurally distinct compounds, scaffold-aware validation can provide medicinal chemistry teams with more realistic performance expectations when prioritizing compounds for experimental follow-up and reduce reliance on potentially overoptimistic model estimates.

Author contributions: Conceptualization, Seyedaryan Mousavi and Aida Hajishafieha; Methodology, Seyedaryan Mousavi and Aida Hajishafieha; Software, Seyedaryan Mousavi and Aida Hajishafieha; Validation, Seyedaryan Mousavi and Aida Hajishafieha; Formal analysis, Seyedaryan Mousavi and Aida Hajishafieha; Investigation, Seyedaryan Mousavi and Aida Hajishafieha; Resources, Seyedaryan Mousavi and Aida Hajishafieha; Data curation, Seyedaryan Mousavi and Aida Hajishafieha; Writing - original draft, Seyedaryan Mousavi and Aida Hajishafieha; Writing - review and editing, Seyedaryan Mousavi and Aida Hajishafieha; Visualization, Seyedaryan Mousavi and Aida Hajishafieha; Supervision, Seyedaryan Mousavi and Aida Hajishafieha; Project administration, Seyedaryan Mousavi and Aida Hajishafieha; Funding acquisition, Seyedaryan Mousavi and Aida Hajishafieha;



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Sciforum-210340: Data-driven identification of potential NDM-1 inhibitors using machine learning and large-scale virtual screening.

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Antimicrobial resistance is one of the most pressing global health challenges, particularly due to the increasing prevalence of multidrug-resistant Gram-negative bacteria. Among the most clinically relevant resistance mechanisms, the metallo-β-lactamase NDM-1 is of particular concern because of its ability to hydrolyze a broad range of β-lactam antibiotics, including carbapenems. Despite its clinical importance, no clinically approved inhibitor is currently available to effectively target this enzyme.

In this study, we developed an integrated computational workflow combining machine learning, large-scale virtual screening, molecular similarity analysis, ADMET profiling, and molecular docking to prioritize potential NDM-1 inhibitor candidates. A curated dataset comprising 3,952 compounds, including 252 active molecules, was assembled from PubChem BioAssays and represented using Morgan fingerprints. An XGBoost classifier was trained and evaluated using stratified cross-validation and an independent test set, achieving strong predictive performance (ROC-AUC = 0.922, PR-AUC = 0.686, MCC = 0.63). Y-randomization experiments further supported model robustness, indicating that the observed predictive performance was not attributable to chance correlations.

The optimized model was subsequently applied as an enrichment filter to approximately 500,000 compounds retrieved from the ZINC and DrugBank databases, reducing the initial chemical space to 98 high-priority candidates. These compounds were further prioritized through Tanimoto-based molecular similarity analysis, ADMET profiling, and molecular docking. D-captopril and meropenem were included as reference compounds to contextualize inhibitor-like and substrate-like interaction patterns within the NDM-1 active site.

This integrated workflow prioritized ten chemically diverse candidates. Among these, LIG-9 and LIG-10 exhibited the most favorable docking scores (-9.64 and -9.49 kcal/mol, respectively) and formed key interactions within the Zn^{2+}-dependent catalytic region of NDM-1. Overall, these findings demonstrate the potential of integrating machine learning with ligand-based and structure-based computational approaches to accelerate the identification and prioritization of novel NDM-1 inhibitor candidates.

Author contributions: Conceptualization, Eduvan Daniel Valencia-Cristancho, Yeison Alberto Garcés-Gómez, Mauricio Galvis Patiño, Lusayda Sanchez-Corrales and Luisa Frenanda Sastoque-Galeano; Methodology, Eduvan Daniel Valencia-Cristancho, Mauricio Galvis Patiño and Luisa Frenanda Sastoque-Galeano; Software, Eduvan Daniel Valencia-Cristancho; Validation, Eduvan Daniel Valencia-Cristancho; Formal analysis, Eduvan Daniel Valencia-Cristancho; Investigation, Eduvan Daniel Valencia-Cristancho and Luisa Frenanda Sastoque-Galeano; Resources, Eduvan Daniel Valencia-Cristancho; Data curation, Eduvan Daniel Valencia-Cristancho and Luisa Frenanda Sastoque-Galeano; Writing - original draft, Eduvan Daniel Valencia-Cristancho; Writing - review and editing, Eduvan Daniel Valencia-Cristancho; Visualization, Eduvan Daniel Valencia-Cristancho, Yeison Alberto Garcés-Gómez, Lusayda Sanchez-Corrales and Luisa Frenanda Sastoque-Galeano; Supervision, Eduvan Daniel Valencia-Cristancho, Yeison Alberto Garcés-Gómez, Mauricio Galvis Patiño and Lusayda Sanchez-Corrales; Project administration, Eduvan Daniel Valencia-Cristancho and Yeison Alberto Garcés-Gómez; Funding acquisition, Yeison Alberto Garcés-Gómez;



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Sciforum-210394: MARSplines-Based QSAR Modeling of Asundexian Derivatives as Factor XIa Inhibitors

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Factor XIa (FXIa) has emerged as an attractive molecular target for the development of anticoagulant agents. The aim of this study was to develop a quantitative structure–activity relationship (QSAR) model describing the inhibitory activity of structurally related asundexian derivatives against FXIa. The analyzed dataset comprised asundexian and 34 derivatives with experimentally reported IC_{50} values, which were converted to pIC_{50}. Three-dimensional molecular structures were prepared in HyperChem and geometry-optimized using the MM+ force field followed by the semi-empirical PM3 method. Molecular descriptors were subsequently calculated using Dragon. Following preprocessing and variable selection, seven descriptors (Eta_sh_x, ITH, H4m, F04[N–O], Mor24u, Gu, and Mor03s) were used to construct a nonlinear QSAR model with Multivariate Adaptive Regression Splines (MARSplines) implemented in TIBCO Statistica 13.3. The resulting model showed a high goodness of fit (R^2 = 0.951) and strong internal cross-validation performance (Q^2LOO = 0.923), with MAELOO = 0.038 and RMSELOO = 0.051. Four of the seven selected variables were three-dimensional descriptors, suggesting that molecular geometry and spatial atomic distribution contribute relevant information to the activity pattern within this congeneric series. The developed model provides an interpretable computational framework for structure–activity analysis of asundexian derivatives and may support the prioritization of structurally related FXIa inhibitors for further experimental investigation.

Author contributions: Conceptualization, Marcin Gackowski; Methodology, Marcin Gackowski; Software, Marcin Gackowski; Validation, Marcin Gackowski; Formal analysis, Michal Janiak and Marcin Gackowski; Investigation, Michal Janiak, Julia Standarska and Marcin Gackowski; Resources, Marcin Gackowski; Data curation, Michal Janiak, Julia Standarska and Marcin Gackowski; Writing - original draft, Michal Janiak, Julia Standarska and Marcin Gackowski; Writing - review and editing, Julia Standarska and Marcin Gackowski; Visualization, Michal Janiak and Marcin Gackowski; Supervision, Marcin Gackowski; Project administration, Marcin Gackowski;



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Sciforum-210431: Bridging a Pharmacopoeial Gap DoE-Optimized RP-HPLC Assay and Dissolution Method Development & Validation for Cefixime–Ofloxacin Fixed-Dose Combination Tablets

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Cefixime (200 mg) and Ofloxacin (200 mg) fixed-dose combination (FDC) tablets have been listed on India's CDSCO-approved formulary since 2010, yet no pharmacopoeia — Indian pharmacopoeia, United State Pharmacopeia, British pharmacopoeia, European pharmacopoeia, or International pharmacopoeia —currently prescribes an official assay or dissolution method for the combination, despite validated methods existing for each drug individually. This work addresses that gap through two linked studies. First, an Analytical Quality by Design (AQbD) approach was used to develop a stability-indicating gradient RP-HPLC assay: an Ishikawa fishbone analysis identified flow rate, column temperature, and buffer pH as critical method parameters, which were optimized using a Box–Behnken Design to achieve baseline resolution ($>$6.8) of both actives within a 10-minute run. The method was validated per ICH Q2 (R2) — linear (R^2 = 1.00), accurate (100.0–100.7% recovery), precise (%RSD $<$ 1%), specific, and robust — and successfully applied to 8 marketed FDC brands, all within the 90–110% label-claim window, with an AGREE greenness score of 0.79. Second, a dissolution method was developed by screening five media, two apparatus types, and three agitation speeds against solubility and disintegration behavior of both BCS Class II (Ofloxacin) and Class IV (Cefixime) actives. Phosphate buffer pH 7.2, USP Apparatus 2 (paddle), 100 rpm, and 45-minute sampling were identified as optimal, achieving ~99% release for both drugs. This method was similarly validated per ICH Q2 (R2) and discriminated compliant from marginal batches across eight marketed formulations. Together, these methods provide the first validated compendial-ready assay and dissolution procedures for this widely prescribed FDC.

Author contributions: Conceptualization, Pushpendu Gaurav; Methodology, Pushpendu Gaurav; Validation, Prashant Tiwari; Formal analysis, Prashant Tiwari; Writing - original draft, Pushpendu Gaurav; Supervision, Sonal Dubey; Project administration, Sonal Dubey;



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Sciforum-210929: Computational Identification of Structural Determinants Associated with Transesterification Activity in Microbial Lipases

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Triacylglycerol acylhydrolases (lipases; EC 3.1.1.3) are versatile enzymes capable of catalysing both hydrolysis and synthetic reactions, including transesterification. Their broad catalytic properties make them valuable biocatalysts for various industrial and pharmaceutical applications. However, despite the availability of thousands of annotated lipase sequences in public databases, the functional characteristics and transesterification potential of many lipases remain poorly understood. Identifying the molecular and structural features associated with transesterification activity is therefore important for improving the functional characterization and prioritization of lipases for further investigation.

In the present study, an integrated computational approach was employed to characterize lipases and identify candidates with potential transesterification activity. Curated lipases with available experimental information were collected and analysed to investigate sequence motifs, conserved residues, and structural characteristics. Comparative analysis of representative lipases was performed to identify functionally important residues, substrate-binding features, and structural architectures associated with transesterification activity. These characteristics were subsequently used to investigate and prioritize poorly characterized lipase candidates. Furthermore, a candidate lipase exhibiting favourable sequence and structural characteristics, particularly substrate-binding features, was identified as a promising candidate for further investigation.

Overall, this study demonstrates that the integration of sequence and structural analyses provides an effective computational strategy for characterizing poorly understood lipases and identifying candidates with potential transesterification activity. The findings contribute to a better understanding of sequence–structure–function relationships in lipases and provide a basis for the computational prioritization of promising biocatalysts for subsequent experimental validation and potential industrial applications.

Author contributions: Methodology, Sahana H; Validation, Sahana H and V S Vidya; Formal analysis, V S Vidya; Writing - original draft, Sahana H; Writing - review and editing, Sahana H, V S Vidya and Saravanan Parameswaran; Supervision, Saravanan Parameswaran; Project administration, Saravanan Parameswaran;



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Sciforum-211015: AI-Assisted Design of a New Chemical Space of Potential Small Molecules Targeting ROR1 in Triple-Negative Breast Cancer

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Introduction. Triple-negative breast cancer is characterized by the absence of ER, PR, and HER2 expression, which necessitates the search for alternative molecular targets. One such target is ROR1, specifically its pseudokinase domain.

Objective. Compare generative AI models based on their ability to generate structurally diverse small molecules with ROR1-targeting potential, and conduct a preliminary computational evaluation of these molecules.

Methods. AI models GPT-5.6 Luna, Gemini 3.5 Flash-Lite, and Claude Sonnet 5.5 were given the same structured prompt based on 130 compounds from four ROR1 studies. Each model generated 10 SMILES strings, which were validated by conversion to molecular graphs. Structural diversity was assessed using the Tanimoto coefficient. Docking was performed in AutoDock Vina v1.2.5 against ROR1 (PDB 6TU9), using ponatinib as the reference ligand.

Results. In-group Tanimoto distance was 0.77±0.13 for ChatGPT, 0.68±0.17 for Claude, and 0.68±0.11 for Gemini-generated sets. The mean Tanimoto similarity to the reference set was 0.23±0.12, 0.29±0.10, and 0.30±0.09, respectively. The average docking scores were -10.38±1.04, -10.27±1.07, and -10.66±0.93 kcal/mol, respectively. Gemini-ROR1-05 exhibited the best docking score (-12.03 kcal/mol, versus -12.44 kcal/mol for ponatinib). Claude-generated molecules outperformed ChatGPT, Gemini, and reference sets based on QED (0.51±0.17; range 0.25–0.77) and SA (2.57±0.17) scores.

Conclusions. All models generated valid and structurally diverse molecules. ChatGPT demonstrated the greatest in-group diversity, while Gemini achieved the best average docking score. These metrics did not reveal a clear advantage for any single model. Some compounds had docking performance close to that of ponatinib, which supports their further validation.

Author contributions: Conceptualization, Anastasiia Ryzhuk, Roman Lesyk and Victoriya Georgiyants; Methodology, Yuliya Prokopenko, Mykola Klishch, Roman Lesyk and Victoriya Georgiyants; Software, Anastasiia Ryzhuk, Yuliya Prokopenko and Mykola Klishch; Validation, Yuliya Prokopenko, Mykola Klishch, Roman Lesyk and Victoriya Georgiyants; Formal analysis, Yuliya Prokopenko and Mykola Klishch; Resources, Yuliya Prokopenko, Mykola Klishch, Roman Lesyk and Victoriya Georgiyants; Data curation, Anastasiia Ryzhuk, Roman Lesyk and Victoriya Georgiyants; Writing - original draft, Anastasiia Ryzhuk; Writing - review and editing, Anastasiia Ryzhuk; Visualization, Anastasiia Ryzhuk and Mykola Klishch; Project administration, Anastasiia Ryzhuk, Roman Lesyk and Victoriya Georgiyants;



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Sciforum-211095: AI-Driven Prediction of Anti-inflammatory Dose Requirements and Treatment Response for Patient-Specific Management of Ulcerative Colitis

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Background

Ulcerative colitis (UC) is a chronic inflammatory bowel disease characterized by patient heterogeneity and variable therapeutic response. Current treatments remain empirical, while drug repurposing offers a promising strategy to accelerate therapeutic development. Vardenafil, a phosphodiesterase-5 inhibitor with anti-inflammatory potential in UC, represents a model repurposed drug.

AimThis study aimed to develop AI-based predictive models for patient-specific management of UC, using vardenafil as a model repurposed drug.

MethodsA dataset of 370 patient records retrospectively curated from published UC studies involving different anti-inflammatory therapies. Animal data were converted to human-equivalent data, where applicable. Patient-specific demographic and clinical characteristics, including age, weight, disease duration, smoking status, family history, Mayo score, C-reactive protein, interleukin-6, and fecal calprotectin, were used as predictive variables. Three machine learning models predicted dose requirement (mg/day), treatment response (0-100%), and the subsequent intervention (no action, dose escalation, or surgery). Several machine learning algorithms were tested to select the ones with the least errors. Models were developed using a 70:30 training/testing split, with cross-validation during hyperparameter optimization. Vardenafil was selected as the model repurposed drug, based on preclinical evidence and model-derived predictions were evaluated in a rat model of UC.

ResultsGradient Boosting demonstrated the strongest performance among algorithms, for the three models. Dose prediction achieved R^2 = 0.984 and RMSE = 0.121 while treatment-response prediction achieved R^2 = 0.730 and RMSE = 12.976. Prediction of intervention achieved an F1-score of 0.845, precision of 0.834, and recall of 0.868. Experimental evaluation showed close agreement between model-derived and observed outcomes, providing preliminary support for predicted treatment effectiveness.

ConclusionAI-driven modelling provides a promising approach for patient-specific prediction of anti-inflammatory dose requirements, treatment response and subsequent intervention in UC. However, prospective clinical validation is required before clinical implementation and to determine whether the approach improves patient outcomes.

Author contributions: Conceptualization, Marwa Hamdy Sayed Dawoud; Methodology, Marwa Hamdy Sayed Dawoud, Ahmed Hussein Mohammed Mohammed, Rana Raef Shaker, Kareem Medhat Abdullah Abdelal and Mariam Osama Hamza; Software, Marwa Hamdy Sayed Dawoud; Validation, Marwa Hamdy Sayed Dawoud; Formal analysis, Marwa Hamdy Sayed Dawoud, Ahmed Hussein Mohammed Mohammed, Rana Raef Shaker, Kareem Medhat Abdullah Abdelal and Mariam Osama Hamza; Investigation, Marwa Hamdy Sayed Dawoud and Ahmed Hussein Mohammed Mohammed; Resources, Marwa Hamdy Sayed Dawoud; Data curation, Marwa Hamdy Sayed Dawoud and Mariam Osama Hamza; Writing - original draft, Marwa Hamdy Sayed Dawoud, Ahmed Hussein Mohammed Mohammed, Rana Raef Shaker, Kareem Medhat Abdullah Abdelal and Mariam Osama Hamza; Writing - review and editing, Marwa Hamdy Sayed Dawoud, Ahmed Hussein Mohammed Mohammed, Rana Raef Shaker, Kareem Medhat Abdullah

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Sciforum-211127: Environmentally Friendly HPLC Method for Two Antidiabetic Agents for Simultaneous Estimation

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Eco-friendly analytical procedure refers to reducing or eliminating the hazardous solvents and reagents used during the analysis of APIs as well as pharmaceuticals by chromatographic technique. The antidiabetic agents sitagliptin phosphate monohydrate and metformin hydrochloride, which are mainly prescribed for the treatment of type 2 diabetes mellitus. The QbD-based method development strategies are rapid, robust, and environmentally sustainable. The instrument, high-performance liquid chromatography, was used during method development and optimised using Design-Expert software to identify critical method parameters with respect to the response of critical analytical attributes. The optimised method used chromatographic conditions with an ambient column oven temperature and a flow rate of 1.15 mL/min. The λ256 nm, the mobile phase 55:45 (v/v) of KH2PO4 and ethanol, the buffer pH 4.50, the column dimensions were 4.6 mm of internal diameter, 250 mm length, and the particle size of the stationary phase was 5 micrometres and 100 angstrom pore size. The optimised method was validated in accordance with the International Council of Harmonisation Q2R1. Therefore, the method is robust and eco-friendly and can quantify both APIs and branded formulations using high-performance liquid chromatography.

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Author contributions: Conceptualization, JAISING TOPPO and Akhilesh Tiwari; Methodology, JAISING TOPPO and Akhilesh Tiwari; Formal analysis, Akhilesh Tiwari; Investigation, Akhilesh Tiwari; Writing - original draft, JAISING TOPPO; Writing - review and editing, JAISING TOPPO and Akhilesh Tiwari; Visualization, Akhilesh Tiwari; Supervision, Akhilesh Tiwari;



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Sciforum-211337: Drug repurposing of FDA-approved Bisantrene and Canagliflozin as potential CHK1 inhibitors: insights from molecular docking and molecular dynamics simulations

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Checkpoint kinase 1 (CHK1) is an essential serine/threonine kinase involved in DNA damage response and cell cycle control. Dysregulated CHK1 activation has been found to be associated with tumor progression and resistance to various therapies in many cancer types and thus is an attractive target for development of anti-cancer drugs. In the present study, we use a structural-based virtual screening approach and screened 3500 FDA-approved drugs retrieved from Drug Bank. The molecular docking studies, which illustrated several potential candidates, showed that both Bisantrene and Canagliflozin achieved higher binding energies (-9.2 and -9.5 kcal/mol, respectively) than the reference inhibitor Prexasertib (-7.5 kcal/mol) according to docking with InstaDock. Interaction profiling showed that these ligands mainly occupied the ATP-binding site, interacting with the crucial catalytic residues (LEU15, GLY16, GLU17, GLY18, TYR20, GLU22, VAL23 and LYS38) through hydrogen bonds, pi-sigma interactions and hydrophobic contacts which implied stable and specific binding modes. Similarly, molecular dynamics simulations for 500 ns with GROMACS indicate studying docked complexes stability by reporting RMSD and overall compactness. PCA and FEL analyses further corroborated that both CHK1-Bisantrene and CHK1-Canagliflozin complexes had similar stability when compared to the CHK1-Prexasertib complex reference. Energy calculations and solvent exposure supported by these favorable binding and structural parameters. These results bring up Bisantrene and Canagliflozin as potential CHK1-binding candidates for repurposing in the form of anticancer drugs and recommended for further validation by *in-vitro* and *in-vivo*.

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Sciforum-211382: In Silico Evaluation of Escitalopram Derivatives for Alzheimer's Disease

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Alzheimer's disease (AD) is the most common form of dementia. The NLRP3 inflammasome, a key mediator of inflammation, plays an important role in AD pathophysiology. Since SSRI derivatives are being investigated as potential therapeutic agents for AD, this study aimed to investigate the activity of escitalopram derivatives against NLRP3. Escitalopram derivatives were identified using SwissSimilarity and filtered according to their predicted ADME and toxicity profiles using SwissADME and pkCSM. The 16 selected compounds were evaluated by molecular docking against NLRP3 (PDB ID: 7ALV) using AutoDock Vina. The protein and ligands were prepared using AutoDock Tools 1.5.6, and docking results were evaluated based on predicted docking scores and ligand-protein interactions. Molecular docking identified compounds **5**, **14**, and **15** as the most promising for binding to NLRP3, with docking scores of -9.2, -8.7, and -8.1 kcal/mol, respectively, compared with -9.7 kcal/mol for the co-crystallized ligand RM5. The reliability of the docking protocol was confirmed by redocking the co-crystallized ligand RM5, with an RMSD value of 0.78 Å. Compounds **5**, **14**, and **15** did not reproduce the same interactions as RM5 but showed favorable interactions within the NLRP3 binding region. Compound **5** established conventional hydrogen bonds with Lys232 and Thr233, a π-cation interaction with His522, a π-π interaction with Trp416, and several hydrophobic interactions. Overall, these results suggest that the selected compounds can interact with NLRP3 through binding modes distinct from RM5, supporting further investigation as potential NLRP3-targeting compounds.

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Sciforum-211430: Data-driven identification of potential multi-target antifungal agents for deep mycoses via machine learning and structural modeling

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Introduction: Deep mycoses are severe fungal infections affecting subcutaneous or deeper tissues, often with high mortality rates, with opportunistic mycoses affecting over 3 million individuals globally. Additionally, neglected fungal pathogens such as *Mucorales*, *Sporothrix* spp., and *Histoplasma* spp. affect vulnerable populations, and lack adequate reporting systems. The treatment of these diseases is increasingly compromised by emerging drug resistance, highlighting the need for novel therapeutic strategies.**Methods**: This study employed a sequential virtual screening pipeline to screen libraries of natural products and investigational drugs. It integrated five biologically grouped QSAR models built using the eXtreme Gradient Boosting (XGBoost) algorithm, followed by pharmacokinetic profiling. Prioritized hits underwent multi-target molecular docking against eight targets and were validated through molecular dynamics (MD) simulations to assess thermodynamic stability.**Results**: The virtual screening and subsequent validations identified Citreoindole and TimTec1_006771, from the COCONUT database, as lead candidates. TimTec1_006771 emerged as the superior hit, exhibiting favorable interactions across multiple targets, including squalene epoxidase, squalene synthase, and exo-β-(1,3)-glucanase.**Discussion**: Molecular dynamics results suggests that TimTec1_006771 is capable of multi-target inhibition, simultaneously disrupting membrane ergosterol biosynthesis and fungal cell wall remodeling. This suggests a synergistic effect that increases the evolutionary barrier against resistance. Furthermore, these candidates occupy “beyond Rule of Five” (bRo5) chemical space, suggesting that larger, rigid scaffolds may improve anchoring within diverse binding sites.**Conclusion**: This research provides a computational framework for developing multi-target therapeutics against fungal pathogens. Future research should prioritize in vitro enzymatic and antifungal validation of these compounds, specially against resistant strains.

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Sciforum-211602: Identification of amino acids associated with the agonist and antagonist activities of flavonoids in the PAS-B cavity of the aryl hydrocarbon receptor using molecular docking modeling and artificial intelligence techniques.

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The aryl hydrocarbon receptor (AHR) responds to hundreds of natural and chemical substances and plays a role in defense against chemical insults and bacterial infections, in the adaptive immune response, and in the development of pathological conditions ranging from inflammatory disorders to neoplasms. Numerous natural, endogenous, and synthetic AHR agonists and antagonists have been discovered—including flavonoids, which can act as selective AHR modulators. Therefore, molecular docking and artificial intelligence techniques were used to determine the interaction of flavonoids with the AHR and to identify the amino acid residues associated with AHR agonist or antagonist activities. Twenty-three flavonoids—secondary metabolites from medicinal plants—were investigated (17 with pure agonist activity and 6 pure antagonists). The crystallographic structure of the AHR (PDB: 7vnh) and the MOE 2019.01 program were used for molecular docking, modeling, and complex visualization. Random Forest (version 2) was used as an artificial intelligence tool for amino acid pattern models. Conserved amino acid residues (Tyr, Phe, and His) were identified; given their conservation, they likely play specific roles within the PAS-B domain cavity of the *Drosophila melanogaster* AHR. The following amino acid residues could contribute to flavonoid binding: His275, Phe279, Met284, Tyr305, Tyr336, and His366. His275 and Tyr305 are associated with antagonist activity, whereas Met284, Tyr336, and His366 are associated with agonist activity. Phe279 is common to both agonist and antagonist activities of flavonoids at the AHR.

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Sciforum-211613: Multimodal Graph Neural Network and Natural Language Processing Model for Antileishmanial Molecule Screening

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Neglected Tropical Diseases, such as leishmaniasis, suffer from a lack of new treatments due to limited interest from the pharmaceutical industry, motivating scalable computational strategies for virtual screening of therapeutic candidates, aiming to reduce the investment barrier in drug discovery. This work presented an integrative Deep Learning framework for the screening of compounds against multiple *Leishmania* species, combining self-supervised molecular representation learning, GPU-accelerated construction of chemical similarity networks, multimodal feature fusion within a custom "MoleculeSAGE" architecture, and semi-supervised active learning. The molecular node embedding fused three complementary views under learnable weights: a graph neural encoder applied to the atom-level molecular graph, a fixed-length fingerprint learned by a Tanimoto-optimized autoencoder, and, for labeled bioactivity data, a bioassay embedding. This embedding combined PubMedBERT encodings of assay descriptions, restructured from free text into categorical fields (e.g., target species, readout method) by a locally run large language model (Qwen 3.5 9B), with a species one-hot vector. The resulting graph comprised 296,646 molecular nodes, 22,050 of them labeled ChEMBL bioactivities and 274,596 unlabeled virtual-library compounds, connected by 6,170,742 edges. Labeled compounds were partitioned via a species-stratified Murcko scaffold split into 17,666 training, 2,193 validation, and 2,191 test compounds. On the test set, the model achieved an MCC of 0.5163, F1-score of 0.7431, and accuracy of 0.7589, with per-species F1 ranging from 0.8476 for *L. major* to 0.5455 for the smaller *L. braziliensis* subset (n=51). Benchmarked against a Random Forest baseline under a shared k-NN applicability-domain, MoleculeSAGE achieved higher out-of-domain F1 in all 30 grid configurations tested and degraded less on average, with F1 falling from 0.777 to 0.658 versus 0.768 to 0.601 for the RF, a roughly 29% smaller drop. Together, these results position the framework as an open, scalable pipeline for accelerating antileishmanial drug discovery in an underfunded research area.

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Sciforum-212890: Objective-Specific Measurement Selection for Mechanistic Assessment of Pharmaceutical UVC Degradation

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Background: Pharmaceutical photodegradation studies often use the same concentration data to predict compound loss and to infer the responsible reaction pathway, although these two objectives may require different measurements. Methods: We evaluated a published mechanistic model for UVC treatment of atenolol, acetaminophen, clofibric acid, and antipyrine. Morris elementary-effects screening ranked ten uncertain inputs separately for atenolol half-life and its superoxide-mediated loss fraction. Local Fisher-information analysis then compared eight candidate measurement strategies at six sampling times under 5%, 10%, and 20% assumed probe error. Results: Half-life was governed primarily by quantum yield, initial dissolved organic matter absorbance, photon intensity, and hydroxyl-radical yield, with mean absolute effects of 76.0, 73.5, 72.6, and 66.8 min, respectively. Mechanistic attribution was instead controlled by an effective radical-termination term and grouped superoxide kinetics. The parent-only Fisher matrix was poorly conditioned (8.93 x 10^7). At 10% assumed error, a six-point hydrogen peroxide series reduced the local standard deviation of log kTT,eff to 0.072 and the condition number to 158; additional parent-based strategies left the target standard deviation between 1.95 and 105. Hydrogen peroxide ranked first at all three assumed error levels. Conclusions: Measurements that improve degradation prediction differ from those that resolve photochemical mechanism. Objective-specific sensitivity analysis followed by information-based design provides a transparent method for prioritizing analytical effort in pharmaceutical degradation studies. The proposed measurements remain to be validated experimentally.



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Session 6. New Modalities in Drug Discovery

Sciforum-210375: Effects of orally administered engineered *E. coli* expressing M-GLP-1 on body weight in a rat model of type 2 diabetes

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Introduction: Type 2 diabetes mellitus involves insulin resistance, β-cell dysfunction, and impaired metabolic homeostasis. GLP-1 receptor agonists improve glycemic control but generally require parenteral administration, while oral peptide delivery is limited by degradation and low bioavailability. Engineered microorganisms may provide an alternative platform for oral administration of peptide-expressing bacterial preparations. We evaluated orally administered *E. coli* engineered to express the recombinant GLP-1 variant M-GLP-1 in a rat model of type 2 diabetes.

Methods: M-GLP-1, generated by adding an *N*-terminal methionine to GLP-1(7–37), was expressed in *E. coli* BL21(DE3). Expression was induced with 200 μM IPTG. Cells were harvested, washed, lyophilized, and resuspended before administration. Male Wistar rats (n=50; 10/group; 7 weeks old) with high-fat diet/streptozotocin-induced type 2 diabetes were assigned to vehicle control, empty-vector *E. coli* control, or E. coli-M-GLP-1 at 1×, 2×, or 3× the therapeutic dose (1× = 2.8×10^5 cells/animal). Preparations were administered by oral gavage twice weekly for 5 weeks. The study was approved by the Local Ethics Committee of Privolzhsky Research Medical University (Protocol No. 06, 29 April 2022).

Results: Body weight was comparable among groups before and after diabetes induction. During treatment, E. coli-M-GLP-1-treated rats showed greater body-weight gain than vehicle and empty-vector controls, with trajectories diverging from day 35. By day 56, mean body weight was approximately 299–301 g in the E. coli-M-GLP-1 groups versus 283–284 g in controls.

Conclusions: Oral E. coli-M-GLP-1 administration altered body-weight trajectories compared with vehicle and empty-vector controls in rats with experimental type 2 diabetes. These data do not establish GLP-1-mediated biological activity or confirm peptide delivery. Further studies are required to determine the metabolic significance and mechanism of the observed effect.

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Sciforum-210534: FDA-approved drugs as probes for mixMD: a pipeline modeled on the identification of cryptic pockets of SARS-CoV-2 3CLpro

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Modern drug discovery relies on identifying biologically relevant, druggable pockets on target surfaces. Current evidence indicates that the majority of these pockets are inherently inducible and remain cryptic prior to ligand binding. Mixed-solvent molecular dynamics (mixMD) is one of the few methods that enables identification of such pockets. Conventionally, mixMD involves deploying one or several small-molecule probes distributed within a polar solvent. However, we identified a limitation in this standard protocol stemming from the topological uniformity of such mixMD setups. So, we utilized the FDA-approved drug database as a source of clinically proven, topologically diverse structural scaffolds. We developed a comprehensive semi-automated pipeline that integrates ligand filtering, protonation, parameterization, and automated molecular system assembly. The preparatory stage was implemented by an automated combination of Open Babel for protonation and RDKit for mass filtering, 3D generation and energy minimization (MMFF94). Ligand parameterization was carried out by a separate script that used ACPYPE (AM1-BCC, GAFF2) for each ligand sequentially. Using GROMACS utilities, a custom script automated box sizing and stochastic probe placement based on user-specified ligand-to-water volume fractions and probe copy numbers. A dedicated auxiliary script processed all ligand topology files to prevent atom-type conflicts during system compilation. The prepared ligand topologies were added to the final system topology file. Subsequent system solvation and equilibration followed conventional protocols for Amber14SB-related systems. This pipeline was used to study 3CLpro of SARS-CoV-2, which is one of the key targets for the development of anti-covid drugs. Importantly, even within a relatively short molecular dynamics simulation, our approach enabled the identification of a previously unreported cryptic pocket located outside the active site of 3CLpro. It demonstrated the ability to bind bazedoxifene, a component of the mixMD solvent, which is a selective estrogen receptor modulator.

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Sciforum-210649: N-Substituted 9-Aminoacridine Derivatives as Promising Antimicrobial Agents: Synthesis, Characterization, and Structure–Activity Relationship.

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Introduction: The increasing prevalence of antimicrobial resistance necessitates development of novel antimicrobial agents with improved efficacy and broader activity spectra. Acridine derivatives particularly 9-aminoacridine have attracted considerable interest as promising antimicrobial pharmacophore. In this study, we have synthesized ten derivatives and evaluated N-substituted 9-aminoacridine derivatives for antibacterial and antifungal activities

Methods: Ten derivatives were synthesized through N-alkylation and characterized using TLC, M.P., UV, FTIR, ^{1}H-NMR, and FABMS. Antibacterial activity was evaluated against selected Gram-positive and Gram-negative bacterial strains using the agar diffusion method, with Gentamicin as the reference standard. Antifungal activity was assessed against *Aspergillus fumigatus, Rhizopus* spp., and *Candida albicans*, using Fluconazole as the reference standard.

Results: Among the synthesized derivatives, PMA exhibited the most potent antibacterial activity, comparable to or greater than Gentamicin against *E-coli, Proteus mirabilis, Enterococcus* spp., and *Staphylococcus aureus*. PPA also demonstrated notable antibacterial activity and showed the highest antifungal activity against *Rhizopus* spp., slightly exceeding that of Fluconazole, while PBrS exhibited comparable antifungal activity. Structure–activity relationship analysis revealed that structural modifications at the 9-amino position significantly influenced antimicrobial potency and activity spectrum.

Conclusion:. Overall, the synthesized ten derivatives of 9-amino Acridine demonstrated promising antimicrobial potential, identifying PMA and PPA as particularly promising candidates for further optimization and evaluation.

Author contributions: Methodology, nadia farah;



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Sciforum-210855: From Conformational Control to GPCR Recognition: Structure-Guided Design of Short Peptide and Peptidomimetic Ligands

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G protein-coupled receptors (GPCRs) remain among the most important drug targets, yet the rational design of short peptide and peptidomimetic ligands is complicated by a central problem: the same conformational flexibility that enables molecular recognition can also reduce selectivity and obscure the bioactive geometry. We therefore explore conformational control as a practical bridge between peptide structural chemistry and GPCR-focused ligand design.

Our approach combines experimental structural information with computational analysis of receptor recognition. Short peptide-derived scaffolds with different degrees of conformational restriction were examined using single-crystal X-ray diffraction and conformational analysis, followed by molecular docking and molecular dynamics in selected GPCR binding pockets. Particular attention was given to pseudo-cyclization, sterically restricted residues, and fluorinated termini as strategies for preorganizing the ligand and modulating the presentation of recognition groups.

Across representative systems, conformational restriction reduced the accessible structural space without eliminating local adaptability. In a CF_3-containing dipeptidomimetic, crystal-derived interaction patterns were compared with first-shell environments sampled in the β_2-adrenergic, dopamine D3, and serotonin 5-HT2A receptors. The receptor models showed that the same substituent can encounter distinct aliphatic, aromatic, and polar microenvironments, emphasizing that useful preorganization must coexist with receptor-dependent adaptation.

These results support a design principle in which short peptide GPCR ligands are treated neither as rigid small molecules nor as unconstrained peptides. Instead, controlled flexibility and experimentally informed preorganization may provide a more rational starting point for developing compact peptide-based GPCR modulators.

Author contributions: Conceptualization, Bojarska Joanna; Methodology, Bojarska Joanna; Software, Bojarska Joanna; Validation, Bojarska Joanna; Formal analysis, Bojarska Joanna; Investigation, Bojarska Joanna; Resources, Bojarska Joanna; Data curation, Bojarska Joanna; Writing - original draft, Bojarska Joanna;



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Sciforum-210977: Effect of pre-incubation time on riboflavin–*candida albicans* interactions prior to photodynamic inactivation assessed by spectrophotometry

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Antimicrobial photodynamic inactivation (aPDI) has emerged as a promising approach for controlling *Candida albicans*, relying on the interaction between a photosensitizer, light, and molecular oxygen to generate cytotoxic reactive oxygen species. Photodynamic efficacy is strongly influenced by photosensitizer availability and its interaction with microbial cells before irradiation, making pre-incubation time a relevant parameter for treatment optimization. Riboflavin is a biocompatible, naturally occurring photosensitizer with favorable photochemical properties; however, the kinetics of its association with fungal cells and the influence of pre-incubation time remain poorly understood.

C. albicans ATCC 10231 suspensions (10^5 CFU/mL) were incubated with 400 µmol L^{-1} riboflavin in a 1:1 (v/v) ratio for different pre-incubation times (30–120 min) in 24-well plates under agitation (~400 rpm) and protected from light. Samples were then centrifuged at 4,000 rpm for 5 min, and riboflavin remaining in the supernatant was quantified spectrophotometrically at 450 nm.

Pre-incubation time markedly influenced riboflavin association with *C. albicans*. After 30 min, approximately 30% of the photosensitizer was associated with fungal cells, increasing to 75% after 60 min. A plateau was reached at 90 min, while at 120 min the available riboflavin was nearly depleted, suggesting that the initial concentration limited further time-dependent association.

Spectrophotometry provided a simple approach to optimize photosensitizer pre-incubation time, avoiding unnecessarily prolonged PS–microorganism contact. This strategy may be extended to other photosensitizers, particularly emerging molecules under investigation for photodynamic applications.

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Sciforum-210988: Mechanically Activated Anticonvulsant Lacosamide: Study of Long-Term Changes in Physico-Chemical and Pharmacokinetic Properties

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Introduction: The development of new drugs typically requires approximately 10–15 years; therefore, the modification of known pharmaceutical molecules using mechanochemistry - a "green" technology enabling controlled alteration of material properties - has become highly relevant. In the context of increasing drug resistance, including that observed in epilepsy, targeted structural modification of compounds is of particular importance. **Aim:** To investigate the effect of high-intensity mechanical loading on the physicochemical properties of lacosamide, a third-generation antiepileptic drug, and to establish the relationship between mechanoactivation, solid-state transformation, and the temporal evolution of properties within the framework of the kinetic theory of strength. **Materials and methods:** Lacosamide powder was subjected to mechanoactivation in a laboratory rotor mill under controlled temperature conditions. The obtained samples were analyzed using static and dynamic light scattering, X-ray powder diffraction (XRD), ATR-FTIR spectroscopy, and principal component analysis (PCA). **Results:** Mechanical treatment induced particle fragmentation, accumulation of crystal lattice defects, and rearrangement of intermolecular interactions, without altering the chemical structure. The temperature curve enabled identification of the elastic and plastic deformation stages. Scanning electron microscopy (SEM) confirmed morphological changes from needle-like crystals to particles with smooth surfaces. A main finding was the experimental confirmation of the long-term evolution of the mechanically activated state over a 37-month observation period. The system did not revert to its initial state but exhibited prolonged thermally activated rearrangement, interpreted within the framework of the S.N. Zhurkov equation as stress relaxation. **Conclusions:** Mechanochemical modification represents a controllable approach for altering the solid-state properties of pharmaceutical substances without changing their chemical nature. The proposed kinetic assessment of the activated state durability is valuable for predicting stability and for the development of novel dosage forms, which is of significant importance for both pharmacy and medicine in general.

Author contributions: Conceptualization, Elena Uspenskaya; Methodology, Ekaterina Kuzmina and Elena Uspenskaya; Software, Elena Uspenskaya; Validation, Elena Uspenskaya; Formal analysis, Elena Uspenskaya; Resources, Elena Uspenskaya; Data curation, Yulia Kirichenko and Ekaterina Kuzmina; Writing - original draft, Yulia Kirichenko; Writing - review and editing, Yulia Kirichenko; Visualization, Ekaterina Kuzmina; Supervision, Elena Uspenskaya; Project administration, Elena Uspenskaya;



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Sciforum-211236: Structure-Activity Relationship in Boronic Acid-Functionalized Zinc(II) Phthalocyanines for the Photoinactivation of Gram-Positive Bacteria

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The rapid emergence of antimicrobial resistance demands innovative therapeutic strategies, such as antimicrobial photodynamic therapy (aPDT). While zinc(II) phthalocyanine (ZnPc) dyes possess photophysical properties, their efficacy is often harmed by low solubility and aggregation in biological media. To overcome these limitations, we explored the functionalization of ZnPcs with boronic acid groups to enhance solubility and promote interactions with bacterial cells. We report the synthesis, structural characterization, and photophysical evaluation of tetra(**1**)-, octa(**2**)-, and octa-fluorinated(**3**)-substituted ZnPcs.

Their antimicrobial efficacy was evaluated against *Staphylococcus aureus* under white light irradiation. The results demonstrated that structural variations significantly impact biological outcomes. When tested alone at 5 and 10 μM, the ZnPcs **1** and **2** successfully inactivated *S. aureus* within 30 to 60 min (light dose 180–270 J cm^{-2}). However, the ZnPc **3** derivative was ineffective even after extended irradiation times, failing to induce bacterial inactivation (60 min, light dose 360 J cm^{-2}) .

To potentiate the photodynamic action, potassium iodide (KI) was introduced as a coadjuvant. KI reacts with reactive oxygen species (ROS) to generate highly toxic and persistent reactive iodine species (RIS) in the microenvironment. The addition of KI produced a remarkable synergistic effect, reducing the inactivation times for both ZnPcs **1** and **2** (15–30 min) and enabled complete photoinactivation for the fluorinated ZnPc **3** within 60 min, even at the lowest tested concentrations.

In conclusion, incorporating boronic acid into ZnPcs preserves their photodynamic efficiency, while the synergistic combination with KI successfully overcomes structural limitations. This approach enables highly efficient photoinactivation of Gram-positive bacteria, demonstrating strong potential for aPDT applications.

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Sciforum-211255: Thioglycerol-Substituted Zinc(II) Phthalocyanines as Antibacterial Agents against *Staphylococcus aureus* and *Escherichia coli*

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The growing concern surrounding antibiotic resistance led to the development of new therapeutic alternatives, among which antimicrobial photodynamic therapy (aPDT) has emerged as a promising approach. This technique requires the presence of oxygen, light and a photosensitizer (PS), in order to produce reactive oxygen species (ROS), responsible for the inactivation of bacteria. Among all the well-known types of PSs, phthalocyanines are among the most promising ones, due to their intense absorption and strong optical properties (e.g., high synglet oxygen quantum yields (Φ_Δ) and photostability). Even so, aggregation is still a drawback that needs to be overcome in these PSs. Thus, the insertion of suitable functional groups in the peripheral positions is demanding to enhance biocompatibility.

This study suggests the use of thioglycerol-containing zinc(II) phthalocyanines (ZnPcs) as PSs to photoinactivate Gram-positive bacteria (*Staphylococcus aureus*) and Gram-negative bacteria (*Escherichia coli*). The two presented PSs (ZnPcs **1** and **2**) were synthesized using microwave assistance, from the derivatized phthalonitriles, and their structures were fully characterized. Their optical properties were studied, which showed high solubility in phosphate buffer saline (PBS) solution, high Φ_Δ (ZnPc **1**, Φ_Δ = 0.50; ZnPc **2**, Φ_Δ = 0.55) and photostability.

In conclusion, these photophysical results showed that the designed phthalocyanines are promising candidates for the aPDT activity against *E. coli* and *S. aureus*. Therefore, further *in vitro* studies will be conducted to evaluate the efficacy of the PSs to photoinactivate the two types of bacteria.

Author contributions: Conceptualization, Leandro M. O. Lourenço; Methodology, Juliana S. F. Cebola and Daiane N. Maronde; Validation, Juliana S. F. Cebola, Daiane N. Maronde, Adelaide Almeida and Leandro M. O. Lourenço; Formal analysis, Juliana S. F. Cebola, Daiane N. Maronde, Adelaide Almeida and Leandro M. O. Lourenço; Investigation, Juliana S. F. Cebola and Daiane N. Maronde; Resources, Adelaide Almeida and Leandro M. O. Lourenço; Writing - original draft, Juliana S. F. Cebola and Daiane N. Maronde; Writing - review and editing, Juliana S. F. Cebola, Daiane N. Maronde, Adelaide Almeida and Leandro M. O. Lourenço; Supervision, Adelaide Almeida and Leandro M. O. Lourenço; Funding acquisition, Adelaide Almeida and Leandro M. O. Lourenço;



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Sciforum-211519: AAV8-Mediated shRNA Knockdown of PCSK9 as Gene Therapy for Dyslipidemia.

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Dyslipidemia and elevated LDL cholesterol are major drivers of atherosclerotic cardiovascular disease. PCSK9 binds hepatic LDL receptors and promotes their degradation; its inhibition increases LDLR recycling and lowers plasma LDL-C. We aimed to develop an AAV8-based gene therapy delivering shRNA for durable PCSK9 silencing. First, human PCSK9 mRNA (NM_174936.3) was analyzed for conserved exons and isoforms. 5 shRNA candidates (19–21 nt, GC 30–50%, no SNPs or predicted off-targets) were designed against CDS/3′UTR. Candidates were cloned into an AAV expression plasmid under U6 promoter between ITRs and verified by colony PCR and Sanger sequencing. Huh7/HepG2 cells were transfected with shRNA plasmids. Knockdown was assessed 48–72 h post-transfection by qRT-PCR, Western blot/ELISA, and MTT. The lead shRNA produced $>$70% reduction in PCSK9 mRNA and decreased secreted PCSK9 without significant cytotoxicity versus negative controls. The verified plasmid was packaged into AAV8 using a three-plasmid HEK293T system with RepCap, helper, and transfer plasmids; vectors were purified by lysis, filtration, PEG precipitation/affinity chromatography, and concentrated. qPCR titration yielded ≥$1\times10^{12\text{-}13}$ genome copies/mL. An AAV8-shRNA vector targeting PCSK9 was successfully designed, validated in vitro, and produced. This platform supports further in vivo testing for stable LDL-C reduction in dyslipidemia.

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Author contributions: Conceptualization, Evgeny E. Bezsonov; Methodology, Evgeny E. Bezsonov; Software, Evgeny E. Bezsonov; Validation, Evgeny E. Bezsonov; Formal analysis, Evgeny E. Bezsonov; Investigation, Evgeny E. Bezsonov; Resources, Evgeny E. Bezsonov; Data curation, Evgeny E. Bezsonov; Writing - original draft, Evgeny E. Bezsonov; Writing - review and editing, Evgeny E. Bezsonov; Visualization, Evgeny E. Bezsonov; Supervision, Evgeny E. Bezsonov; Project administration, Evgeny E. Bezsonov; Funding acquisition, Evgeny E. Bezsonov;



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Session 7. Radiopharmaceuticals

Sciforum-211126: Optimizing the Dissociation Rate constant of ^{64}Cu-labeled Nectin-4-Targeting Bicyclic Peptides to Prolong Tumor Retention

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Nectin-4 is a cell adhesion protein with a high abundance in various tumor entities, in particular urothelial carcinoma (UC) including bladder cancer. Its suitability as a therapeutic target has been proven by the clinically approved antibody-drug conjugate enfortumab vedotin. Recently, radiolabeled peptidic probes for molecular imaging emerged, but their potential for radioligand therapy remains limited due to insufficient tumor retention. The present study aimed at reducing the dissociation rate constant (k_{off}) of our previously developed ligand **NECT-224** to potentially prolong the tumor retention.

Starting from the peptidic scaffold of **NECT-224**, a series of analogs bearing a single amino acid substitution in position 3 (dAsp), was synthesized via solid-phase peptide synthesis. Binding constants toward recombinant human Nectin-4 were determined by surface plasmon resonance interaction analysis. Peptides with the lowest k_{off} values were chosen for conjugation of the radiometal chelator (*R*)-NODAGA. The resulting compounds **NECT-458** (dPhe^3) and **NECT-460** (dTrp(5OH)^3) were radiopharmacologically characterized upon labeling with ^{64}Cu using the HT-1376 urothelial cancer model *in vitro* and *in vivo* by small-animal PET/CT imaging up to 24 h p.i.

Compared to **NECT-224** with a k_{off} value of , **NECT-460** and **NECT-458** exhibited reduced k_{off} values (). This resulted in lower dissociation constants (K_d) towards recombinant Nectin-4 () and comparable on HT-1376 cells () as compared to **NECT-224** (). PET/CT imaging in HT-1376 tumor-bearing mice revealed a significantly longer tumor retention for both ^{64}Cu-labeled peptides compared to **[^{64}Cu]Cu-NECT-224**, which enabled even a clear tumor visualization at 24 h p.i.

These findings support our hypothesis that lowering the dissociation rate constant is an effective strategy for improving the tumor retention within this series of Nectin-4-targeting bicyclic peptides and suggest that k_{off} can guide the selection of candidates for further theranostic radioligand development.

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Session 8. Nanomedicine and Nanotechnology

Sciforum-184990: Effects of Nano-Quercetin on Cypermethrin Induced Liver Injury in Rabbits

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Cypermethrin is a synthetic pyrethroid reported to cause hepatic toxicity and other fatalities in humans as well as animals/birds. Quercetin is a flavonoid that has beneficial health-protective effects, but its use is limited because of its poor bioavailability, metabolism through colonic microbial flora, and first-pass hepatic metabolism. To overcome these limitations, quercetin was loaded into chitosan nanoparticles by following the solvent evaporation method. The study objectives were synthesizing, characterizing quercetin-loaded chitosan nanoparticles, and determining their hepatoprotective potential against chemical (pyrethroid)-induced liver injury in an animal model. The nanoparticles were characterized by zeta size and potential, polydispersity index (PDI), entrapment efficiency, and FTIR. The prepared nano-formulation was physically stable and fell within the nanoscale range (188.5 nm) with high entrapment efficiency (80.4%). The rabbit model was selected because its hepatic metabolic pathways and lipid profile closely resemble those of humans, and no validated in vitro or computational model exists that can adequately replicate the systemic, dose-dependent hepatotoxic response of cypermethrin required to evaluate the nanoformulation's protective efficacy in vivo. In accordance with the 3Rs principles, the sample size (n = 5/group) was statistically determined as the minimum required to achieve reliable and reproducible results, thereby minimizing animal use (Reduction), while animals were housed under standardized conditions with regular monitoring and humane endpoints to minimize distress (Refinement); Ethical approval was taken from ethical committee of University of Agriculture, Faisalabad vide approval No. 2473/ORIC. The study was conducted with four treatment groups (n = 5) comprising 20 rabbits: group 1 was the negative control (normal diet), group 2 was the positive control (cypermethrin 24 mg/kg), and groups 3 and 4 were treated with low-dose (10 mg/kg) and high-dose (20 mg/kg) quercetin-loaded chitosan nanoparticles, respectively, along with cypermethrin (24 mg/kg) for 28 days. Cypermethrin-treated animals showed elevated liver function test (LFT) levels and histopathological lesions in the liver. Co-administration of quercetin-loaded chitosan nanoparticles with cypermethrin successfully ameliorated hepatotoxicity in a dose-dependent manner.



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Sciforum-209008: Development of a specific magnetic support for tetanus toxoid separation

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Magnetic separation is currently gaining significant attention as a process in the biotechnology industry. The innovative solutions offered by this methodology for separating analytes of interest have advanced beyond the analytical scale. The complexity of this technique lies in developing an optimal separation support for the system in question. Considering that tetanus toxoid is part of a wide range of products in the pharmaceutical industry, such as conjugate vaccines based on tetanus toxoid as a carrier protein, the development of selective magnetic separation techniques for tetanus toxoid represents a novel alternative. For this reason, in this work, a magnetic support was developed based on anti-tetanus toxoid antibody immobilized on iron oxide nanoparticles. The nanoparticles were obtained by coprecipitation and post-synthesis modification with polyacrylic acid and gallic acid. The antibody immobilization was carried out through interaction with protein G, which was previously anchored to the nanoparticles. The nanoparticles were characterized by X-ray Diffraction, Infrared Spectroscopy, Transmission Electron Microscopy, Scanning Electron Microscopy, Thermogravimetry, Vibrating Sample Magnetometry, Dynamic Light Scattering, and Zeta Potential. The obtained nanoparticles showed a diffraction pattern corresponding to magnetite, a morphology of aggregated spheres with a particle size of 13 nm, and stability in aqueous suspension. The covalent anchoring of protein G was evaluated through colorimetry and SDS-PAGE Electrophoresis. The functionalized nanoparticles with protein G were able to immobilize tetanus toxoid antibody through interaction in an aqueous medium.

Author contributions: Conceptualization, Marcos Muñoz Arias; Methodology, Glenda Bauta Castañeda , Marcos Muñoz Arias and Daniel Díaz Casas ; Validation, Jean Pierre Soubal; Formal analysis, Glenda Bauta Castañeda and Marcos Muñoz Arias; Investigation, Glenda Bauta Castañeda , Marcos Muñoz Arias and Daniel Díaz Casas ; Resources, Alicia M. Díaz-García; Data curation, Glenda Bauta Castañeda ; Writing - original draft, Glenda Bauta Castañeda ; Writing - review and editing, Glenda Bauta Castañeda ; Visualization, Marcos Muñoz Arias, Jean Pierre Soubal, Darielys Santana and Alicia M. Díaz-García; Supervision, Marcos Muñoz Arias, Daniel Díaz Casas and Alicia M. Díaz-García; Project administration, Darielys Santana and Alicia M. Díaz-García;



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Sciforum-209157: Adsorption of paclitaxel onto magnetic nanoparticles for potential application in the treatment of triple-negative breast cancer.

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The chemotherapeutic agent paclitaxel is used in the treatment of triple-negative breast cancer. However, its formulation (Taxol®) exhibits high toxicity and poor targeting. A novel solution involves nanostructured systems based on magnetic iron oxide nanoparticles (IONPs) combined with chemotherapeutic agents. These systems show increased targeting and inhibitory action toward cancer cells, proving to be favorable for developing formulations with anticancer activity. For this reason, in this work, a system based on paclitaxel adsorbed onto chitosan-coated iron oxide nanoparticles was obtained for the treatment of triple-negative breast cancer. IONPs were synthesized via the Massart coprecipitation method and functionalized with chitosan using *in-situ* and post-synthesis methods. They were characterized by XRD, FTIR, TEM, SEM, TGA, DLS, and ζ-Potential. The cell viability of the different systems was studied at various time intervals. The obtained nanoparticles exhibited a diffraction pattern corresponding to magnetite. The presence of chitosan was corroborated by infrared spectroscopy. It was determined that the system obtained via the *in-situ* method was the most appropriate for paclitaxel immobilization and subsequent administration, according to DLS, ζ-Potential, and cell viability profiles. The adsorption kinetics of paclitaxel were studied. The optimal adsorption time was found to be between 2 and 4 hours. The kinetic data fitted the pseudo-second-order model. The drug adsorption isotherm fitted the Freundlich model, evidencing a heterogeneous adsorbent surface with exponentially distributed active site energies.

Author contributions: Conceptualization, Yu Cai and Alicia M. Díaz-García; Methodology, Glenda Bauta Castañeda, Carmen Soto Febles, Lissette Agüero Luztonó and Alicia M. Díaz-García; Software, Dahysmer Hernández Ricardo, Glenda Bauta Castañeda, Marcos Muñoz-Arias and Alicia M. Díaz-García; Validation, Glenda Bauta Castañeda and Alicia M. Díaz-García; Formal analysis, Dahysmer Hernández Ricardo, Glenda Bauta Castañeda, Marcos Muñoz-Arias, Carmen Soto Febles and Alicia M. Díaz-García; Investigation, Dahysmer Hernández Ricardo, Glenda Bauta Castañeda, Marcos Muñoz-Arias, Carmen Soto Febles, Lissette Agüero Luztonó and Alicia M. Díaz-García; Resources, Glenda Bauta Castañeda, Marcos Muñoz-Arias and Alicia M. Díaz-García; Data curation, Dahysmer Hernández Ricardo, Glenda Bauta Castañeda, Marcos Muñoz-Arias and Alicia M. Díaz-García; Writing - original draft, Dahysmer Hernández Ricardo, Glenda Bauta Castañeda and Alicia M. Díaz-García; Writing - review and editing, Glenda Bauta Castañeda and Alicia M. Díaz-García; Visualization, Yu Cai and Alicia M. Díaz-García; Supervision, Glenda Bauta Castañeda and Alicia M. Díaz-García; Project administration, Alicia M. Díaz-García; Funding acquisition, Marcos Muñoz-Arias and Alicia M. Díaz-García;



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Sciforum-209590: Nanomedicine: Emerging Technologies for Advanced Healthcare

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Innovative methods for the molecular and cellular diagnosis, treatment, and prevention of diseases have made nanotechnology a game-changer in contemporary medicine. Utilizing manufactured nanoscale materials as nanomedicine/nanodrug improves patient outcomes and treatment efficacy. Drugs, genes, proteins, and other therapeutic agents can be delivered to particular tissues or cells using nanoparticles such as liposomes, polymeric nanoparticles, dendrimers, metallic nanoparticles, and lipid-based nanocarriers. This focused strategy can improve medication stability and solubility, boost bioavailability, lessen systemic toxicity, and allow for controlled or prolonged drug release. Furthermore, by creating extremely sensitive biosensors, imaging agents, and nanoscale diagnostic platforms that can identify illnesses early on, nanotechnology has made a substantial contribution to diagnostic applications. Additionally, nanomaterials are being investigated for use in vaccine delivery, regenerative medicine, cancer therapy, antimicrobial treatment, and customized healthcare. Notwithstanding these encouraging developments, issues like the toxicity of nanoparticles, biodegradability, immunological reactions, industrial scalability, legal constraints, and long-term environmental effects continue to be significant factors. For nanomedicine to be safe, effective, and clinically applicable, multidisciplinary research must continue. All things considered, the fusion of biomedical research with nanotechnology offers a potential route toward more accurate, effective, and customized treatment. Future advancements in stimuli-responsive delivery systems, smart nanocarriers, and multifunctional nanoparticles may increase the promise of nanomedicine and lead to better treatment outcomes and disease management.



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Sciforum-210160: Design and Evaluation of Granzyme-B Loaded Albumin Nanoparticles for Cancer Immunotherapy

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Immunotherapy has been presented as a less invasive alternative for cancer treatment. However, the efficacy of immunotherapy may be compromised by challenges associated with drug administration, the compatibility of treatment with the patient, and the immunosuppressive nature of the tumor microenvironment. Granzyme B is a serum protease whose main function is to induce the death of target cells that are recognized by cytotoxic T lymphocytes. Various studies demonstrate the role of granzyme B in autoimmune diseases and in cancer therapy. One of the main obstacles to the efficient therapeutic use of this enzyme is the need for protected transport and targeted delivery to the intracellular environment. To overcome these limitations, in this study, human serum albumin (HSA) nanocages were designed as a vehicle for the delivery of granzyme B for application in cancer immunotherapy. Protein nanoparticles (HSA:GrB) were successfully synthesized by reduction intramolecular disulfide bonds of HSA and were characterized by transmission electron microscopy (TEM), dynamic light scattering (DLS) and enzyme activity assays. With an average particle size of 40 nm, the encapuslated granzyme B presented improved stability in enzyme activity, with an encapsulation of active enzyme efficiency of 52%. Successful cellular internalization of HSA:GrB in MDA-MB-231 cell line was confirmed by confocal microscopy. H_2O_2 was used as an oxidizing agent to break the HSA:GrB disulfide bonds allowing the contact between GrB and the intracellular enviroment. Cell viability assay revealed a cytotoxic effect in MDA-MB-231 (24.49% of viability) after treatment with HSA:GrB followed by H_2O_2 treatment (15 min, 3mM) to accelerate the disassembly of the nanoparticles intracellularly, while the cells treated only with 3 mM H_2O_2 and free GrB did not show statistically significant differences with the negative control (untreated cells). HSA:GrB in its highest concentration without H_2O_2 showed 60% of cellular viability. These results confirm the encapsulation efficiency and preservation of the enzymatic activity of granzyme B, the successful intracellular delivery of Granzyme B, as well as its cytotoxic effect on breast cancer cells, demonstrating its immunotherapeutic potential in cancer treatment.

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Author contributions: Methodology, Pabela Maria Barraza Duarte and Kanchan Chauhan; Validation, Kanchan Chauhan; Investigation, Pabela Maria Barraza Duarte and Kanchan Chauhan; Resources, Kanchan Chauhan; Data curation, Pabela Maria Barraza Duarte; Writing - original draft, Pabela Maria Barraza Duarte; Writing - review and editing, Kanchan Chauhan; Supervision, Kanchan Chauhan; Funding acquisition, Kanchan Chauhan;



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Sciforum-210289: The role of Surface Tension Measurement in Lipid Nanoparticle Formulation

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Solid lipid nanoparticles (SLN) are attractive nanocarriers for drug delivery and diagnostic applications. Their formulation requires surfactants that reduce interfacial tension and form a protective layer around the nanoparticles, controlling particle size distribution and ensuring dispersion stability. However, both insufficient and excess surfactant concentrations can promote aggregation, through incomplete interfacial coverage and micellisation-induced surfactant depletion, respectively. This work highlights surface tension measurement as a screening test for selecting the optimal surfactant concentration during SLN formulation.

SLN were prepared by hot melt emulsification method with 1% Compritol ATO888 as the lipidic matrix. Poloxamer 407 and soy lecithin were used as surfactants, either individually or in 1:1 ratio. The surfactant concentrations were ranged from 0.02 to 2% (m/v). Particle size (PS) and polydispersity index (PDI) were assessed by Dynamic Light Scattering (DLS) at 25°C.

The surface tensions of SLN dispersions and those of aqueous surfactant solutions were investigated with Du Noüy ring method at 25°C and 45 °C. Critical micelle concentrations (CMC) were determined graphically.

Surface tension measurements indicated distinct thermal behavior among the surfactants, with lecithin exhibiting greater temperature sensitivity at 45°C, decreasing by 0.55 mN/m per °C. The CMC determination for the individual surfactant solutions and their 1:1 mixture revealed a mild antagonism, which may limit surface adsorption at the particle interface. Consistent with this, SLNs prepared with a 0.02% surfactant mixture exhibited a particle size of 246±1.5 nm and higher surface tension than the corresponding surfactant mixture solutions. Furthermore, the evolution of SLN PS and PDI as a function of surfactant mixture concentration remained stable at concentrations between 0.15–0.5%, and increased significantly above 0.5%, suggesting the potential presence of micelles.

These findings provide insight into the surface phenomena affecting SLN stability and offer a rational basis for selecting the optimal surfactant concentration.



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Sciforum-210351: Green-Synthesized Ag, ZnO, and CuO Nanoparticles: From Formation and Characterization to Biomedical Potential

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Green synthesis of metal and metal oxide nanoparticles using plant extracts represents a sustainable and environmentally friendly approach to obtaining functional nanomaterials with potential biomedical applications. Plant extracts are complex sources of bioactive compounds that may participate in nanoparticle reduction, formation, and stabilization, while the nature of the metal and synthesis conditions significantly influence nanoparticle formation and the properties of the resulting nanosystems. **This study experimentally compares the green synthesis and physicochemical characteristics of silver (Ag), zinc oxide (ZnO), and copper oxide (CuO) nanoparticles, while their biomedical potential is discussed in the context of previously published biological studies.**

Nanoparticle formation was monitored by UV–Vis spectroscopy, while interactions between plant-derived biomolecules and the formed nanoparticles were investigated using FTIR spectroscopy. Particle morphology and size were determined by TEM analysis. Comparative evaluation revealed differences among Ag, ZnO, and CuO systems in terms of formation behavior, morphology, particle size, and stability. Silver was predominantly obtained as elemental Ag nanoparticles, whereas zinc and copper preferentially formed ZnO and CuO nanoparticles due to their greater susceptibility to oxidation.

The biomedical potential of the investigated nanosystems was comparatively discussed based on previously published studies, including available data on antitumor, antimicrobial, hemolytic, genotoxic, and antigenotoxic activities. This literature-based comparison was used to relate differences in nanoparticle composition and physicochemical characteristics to their reported biological effects. By integrating the experimental findings on green synthesis and physicochemical characterization with previously reported biological data, this comparative approach provides insight into how differences in nanoparticle composition, formation, and properties may influence their biomedical potential.



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Sciforum-210546: Formulation and evaluation of polymeric micelles loaded *in situ* ophthalmic gel of celecoxib

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PURPOSE

Celecoxib is a promising therapeutic agent for retinal inflammatory disorders due to its anti-inflammatory, anti-VEGF, and antiproliferative activities. However, its poor aqueous solubility limits ocular bioavailability. This study aimed to develop a celecoxib-loaded polymeric micelle in situ ophthalmic gel to enhance precorneal retention and corneal permeation with prolonged ocular delivery.

METHODOLOGY

Poloxamer 188 and Poloxamer 407 were screened with different surfactants, namely Tanscutol P , Tween 80 and Span 60, either alone or in combination. Preformulation studies identified the optimum surfactant–polymer combination using the required hydrophilic–lipophilic balance (RHLB) approach. Critical micellar concentration was determined using the pyrene fluorescence probe method. Celecoxib-loaded polymeric micelles were prepared by thin-film hydration using Poloxamer 407, Span 60, and Tween 80 and evaluated for particle size, polydispersity index, zeta potential, entrapment efficiency, drug loading, and in vitro drug release. The optimized formulation was selected using Pareto and desirability function analyses and incorporated into a gellan gum-based ion-activated in situ gel. The formulation was evaluated for physicochemical properties, morphology, drug release, *ex vivo* transcorneal permeation, histopathology, and stability.

RESULTS

At RHLB 10 (Poloxamer407: Span60: Tween 80 = 5.3:1.2:0.5), optimized micelles (Poloxamer407: Span60: Tween 80:Drug = 5.3:1.2:0.5:1) exhibited 98% ± 0.05 entrapment efficiency, 81.23 ± 0.05% drug loading, 53.3 nm particle size, low PDI, and -29.4 mV zeta potential. The *in situ* gel showed 99.91% ± 0.08 optical transparency and viscosities of 246 and 376 cP at room and body temperatures, respectively.Drug diffusion and permeation studies were performed using 1 mL of celecoxib *in situ* gel containing 0.03% w/v celecoxib. The *in vitro* diffusion study using a dialysis membrane demonstrated a cumulative drug diffusion of 0.065 mg/cm^2 at 5 h, whereas the *ex vivo* permeation study using goat cornea showed a cumulative drug permeation of 0.147 mg/cm^2 at 5 h. Histopathology indicated no significant tissue damage.

CONCLUSION

The developed formulation demonstrated stability, ocular biocompatibility, enhanced corneal permeation, and prolonged drug release, supporting its potential as a promising approach for ocular delivery of celecoxib.

Author contributions: Conceptualization, Sayani Bhattacharyya; Methodology, Varsha K R; Validation, Sayani Bhattacharyya; Formal analysis, Varsha K R; Investigation, Varsha K R; Data curation, Varsha K R; Writing - original draft, Varsha K R; Writing - review and editing, Sayani Bhattacharyya; Supervision, Sayani Bhattacharyya; Project administration, Sayani Bhattacharyya;



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Sciforum-210871: An Adapted Synthesis Method and Physicochemical Characterization of Colloidal Silver Dispersions for Prospective Biocidal Materials

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Introduction. The growing resistance of microorganisms to conventional antimicrobial agents has intensified interest in colloidal silver dispersions as alternative biocidal systems. Their functional properties are strongly governed by particle size, morphology, surface state, and aggregation behavior, all of which depend on synthesis and stabilization conditions. This study **aimed** to develop a laboratory-adapted glucose–citrate method for the preparation of a starch-stabilized colloidal silver dispersion and to characterize its physicochemical properties. Silver nanoparticles were synthesized by sequential addition of 0.1 M glucose, sodium citrate, and starch to a 2 mM $AgNO_3$ solution at 60 °C under continuous stirring. The synthesis was performed for 30 min, and aliquots were collected every 5 min for in situ analysis by UV–Vis spectrophotometry, Fourier-transform infrared spectroscopy (FTIR), scanning electron microscopy (SEM), dynamic light scattering (DLS), and electrophoretic light scattering. **Results.** A distinct surface plasmon resonance band was observed at 400–450 nm. Its intensity increased linearly with synthesis time (=0.999), indicating progressive nanoparticle formation. FTIR spectra supported starch adsorption on the nanoparticle surface. SEM revealed predominantly spherical particles with diameters of 50–100 nm. DLS showed a dominant hydrodynamic diameter of approximately 10 nm, a low polydispersity index (0.02), and a zeta potential of -46.7 mV, indicating high colloidal stability. **Conclusions.** The proposed protocol yields a stable, narrowly dispersed silver nanoparticle formulation and may provide a useful basis for developing biocidal materials. Further studies should assess antimicrobial activity, cytotoxicity, storage stability, and the relationship between physicochemical characteristics and biocidal performance.

Author contributions: Conceptualization, Anton Vladimirovich Syroeshkin; Methodology, Elena Valer'evna Uspenskaya; Investigation, Denis Valeryevich Antonov; Data curation, Denis Valeryevich Antonov; Writing - original draft, Denis Valeryevich Antonov; Writing - review and editing, Anton Vladimirovich Syroeshkin; Supervision, Elena Valer'evna Uspenskaya;



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Sciforum-210947: Dynamic Light Scattering Detects Reproducible Process-Associated Shifts in Virus-Like Particle Size Profiles

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Virus-like particles (VLPs) are complex nanoscale structures whose physicochemical characteristics can be affected by processing conditions. Particle-size distribution is therefore an informative parameter for monitoring the physical state and consistency of VLP preparations. In this study, dynamic light scattering (DLS) was evaluated as a rapid method for comparative characterization of VLP size profiles. Ten VLP preparations were analyzed using a Malvern Zetasizer, with seven replicate measurements performed for each preparation. The dominant intensity-weighted particle-size maximum ranged from 111.5 to 165.9 nm across the complete dataset. Within-preparation coefficients of variation ranged from 1.7% to 5.7%, indicating good repeatability of the measurements. Three matched pairs representing two defined processing states were available for direct comparison. In all three pairs, a consistent shift of the dominant particle-size maximum toward smaller diameters was observed: from 141.4 to 113.5 nm, from 150.0 to 113.1 nm, and from 149.9 to 117.0 nm. These changes corresponded to decreases of 19.7%, 24.6%, and 22.0%, respectively, with a mean relative shift of 22.1%. The results show that DLS can detect reproducible process-associated changes in the physical size profile of VLP preparations. Thus, DLS may serve as a rapid complementary tool for process development, comparability assessment, and routine physicochemical characterization of VLP-based biopharmaceuticals.

Author contributions: Conceptualization, Oleg Vladimirovich Ledenev, Tatiana Vladimirovna Grebennikova and Anton Vladimirovich Syroeshkin; Methodology, Oleg Vladimirovich Ledenev, Tatiana Vladimirovna Grebennikova and Anton Vladimirovich Syroeshkin; Software, Oleg Vladimirovich Ledenev, Tatiana Vladimirovna Grebennikova and Anton Vladimirovich Syroeshkin; Validation, Oleg Vladimirovich Ledenev, Tatiana Vladimirovna Grebennikova and Anton Vladimirovich Syroeshkin; Formal analysis, Oleg Vladimirovich Ledenev, Tatiana Vladimirovna Grebennikova and Anton Vladimirovich Syroeshkin; Investigation, Oleg Vladimirovich Ledenev, Tatiana Vladimirovna Grebennikova and Anton Vladimirovich Syroeshkin; Resources, Oleg Vladimirovich Ledenev, Tatiana Vladimirovna Grebennikova and Anton Vladimirovich Syroeshkin; Data curation, Oleg Vladimirovich Ledenev, Tatiana Vladimirovna Grebennikova and Anton Vladimirovich Syroeshkin; Writing - original draft, Oleg Vladimirovich Ledenev, Tatiana Vladimirovna Grebennikova and Anton Vladimirovich Syroeshkin; Writing - review and editing, Oleg Vladimirovich Ledenev, Tatiana Vladimirovna Grebennikova and Anton Vladimirovich Syroeshkin; Visualization, Oleg Vladimirovich Ledenev, Tatiana Vladimirovna Grebennikova and Anton Vladimirovich Syroeshkin; Supervision, Oleg Vladimirovich Ledenev, Tatiana Vladimirovna Grebennikova and Anton Vladimirovich Syroeshkin; Project administration, Oleg Vladimirovich Ledenev, Tatiana Vladimirovna Grebennikova and Anton Vladimirovich Syroeshkin; Funding acquisition, Oleg Vladimirovich Ledenev, Tatiana Vladimirovna Grebennikova and Anton Vladimirovich Syroeshkin;



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Sciforum-210984: Opuntia ficus-indica-Loaded Chitosan/Zinc Oxide Nanocomposites: Physicochemical Characterization, Antibacterial, Antioxidant and Photocatalytic Degradation Investigation

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The present study focuses on developing *Opuntia ficus indica* (*OFI*) loaded chitosan/zinc oxide (CS/ZnO) nanocomposites. Box-Behnken design was used to optimize and analyse the formulation conditions. The physicochemical nature of the prepared nanocomposite was examined and confirmed using XRD, FTIR, SEM coupled with EDS, and TEM. The formulations exhibited significant radical-scavenging activity in both DPPH and ABTS assays, with CS/*OFI*-ZnONCs showing markedly lower IC_{50} (DPPH – 140 µg/mL, ABTS – 185 µg/mL) values than ZnONPs, *OFI*, and *OFI*-ZnONPs, indicating enhanced antioxidant activity. The formulations also demonstrated concentration-dependent antibacterial activity against *Escherichia coli* and *Psuedomonas aeruginosa*, with CS/*OFI*-ZnONCs exhibiting the highest zone of inhibition of 18.33 ± 1.15 mm and 17.33 ± 0.58 mm at 300 µg/mL, respectively. In photocatalytic degradation studies, CS/*OFI*-ZnONCs demonstrated excellent methylene blue degradation efficiency of 96.03% after 50 min of visible-light irradiation, significantly outperforming *OFI*-ZnONPs (80.23%) and *OFI* extract (61.12%). The enhanced photocatalytic performance was further supported by the highest apparent rate constant (0.02957 min^{-1}), which was 2.16- and 1.44-fold higher than those of *OFI* extract and *OFI*-ZnONPs, respectively. Overall, the findings demonstrate that incorporating *OFI*-derived bioactive constituents and ZnO nanoparticles into chitosan produces a multifunctional nanocomposite with enhanced antioxidant, antibacterial, and photocatalytic properties, highlighting its promising potential for sustainable environmental and functional material applications.

Author contributions: Conceptualization, Manali Ashok Vaidya and Shailendra Shivaji Gurav; Methodology, Manali Ashok Vaidya and Shailendra Shivaji Gurav; Software, Manali Ashok Vaidya; Validation, Manali Ashok Vaidya;



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Sciforum-211013: Development of Curcumin–Silver Nanoparticle-Loaded PVA/Starch Nanocomposite Films for Antibacterial Wound Dressing Applications

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Abstract

Curcumin is a natural polyphenol with broad-spectrum antibacterial, anti-inflammatory, antioxidant, and other pharmacological properties. However, its therapeutic potential is limited by poor water solubility, chemical instability, and low bioavailability. Nanotechnology offers a promising approach to overcome these limitations and enhance its antimicrobial activity. In this context, hybrid silver/curcumin nanoparticles (Cur-AgNPs) represent an attractive strategy combining the intrinsic antibacterial properties of silver with the multifunctional activity of curcumin. In this study, Cur-AgNPs were synthesized through a green approach using curcumin as both a reducing and stabilizing agent and their incorporation into biodegradable nanocomposite films based on PVA and potato starch, intended for antibacterial active wound dressing applications. Three formulations were prepared by varying the concentration of silver nitrate ($AgNO_3$) and curcumine in order to investigate its influence on nanoparticle formation and physicochemical properties. The resulting nanoparticles were characterized by UV–Visible and FTIR spectroscopy to evaluate their optical and chemical properties, while dynamic light scattering and zeta potential measurements were performed to determine nanoparticle size and colloidal stability.

Subsequently, the Cur-AgNPs were incorporated into biodegradable nanocomposite films based on polyvinyl alcohol (PVA) and potato starch, with the aim of developing an antibacterial active wound dressing. The antibacterial activity of the resulting systems was evaluated against five clinically relevant Gram-positive and Gram-negative bacterial strains. The Cur-AgNPs demonstrated significant antibacterial activity, which may be attributed to the combined effects of silver and curcumin, as well as the enhanced interfacial interactions associated with their nanoscale dimensions. Incorporation of the Cur-AgNPs into biodegradable PVA/starch films further highlights their potential as sustainable antimicrobial materials for wound-dressing applications. Overall, this green synthesis approach provides a simple and potentially sustainable strategy for the development of curcumin-functionalized silver nanoparticles and their incorporation into biodegradable nanocomposite films with promising potential for antibacterial wound care.

Author contributions: Conceptualization, Farida Bouanani; Methodology, Farida Bouanani; Formal analysis, radjaa slimaneturki; Writing - original draft, dalila ziouet; Visualization, dalila ziouet; Supervision, hayet Belarbi;



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Sciforum-211148: Preparation and Optimization of Favipiravir-Loaded Chitosomes for Intranasal Administration

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The aim: This study aimed to prepare and optimize favipiravir-loaded niosomes (FAV-NIOs) for the treatment of neurotropic viruses in CNS, followed by coating with chitosan to prepare FAV-loaded chitosomes (FAV-CS) for intranasal administration to overcome the low solubility and bioavailability of FAV.

Methods: FAV-NIOs were prepared using the ethanol injection method [1]. The impact of Span® 60 amount (X1) and cholesterol amount (X2) on Z-average, Polydispersity index (PDI), zeta potential (ZP) and encapsulation efficiency (EE%) was evaluated using a 3^2 factorial design. After that, different concentrations of chitosan were used to prepare FAV-CS [2]. The optimized formulations were characterized in terms of colloidal properties, mucoadhesive properties, *in vitro* blood-brain barrier permeability (BBB-PAMPA), *in vitro* drug release, *ex vivo* nasal permeability and biopharmaceutical aspects.

Results: The optimized formulations; FAV-NIO and FAV-CS-0.5 showed Z-average $<$ 300 nm, PDI $<$ 0.3, ZP $>$ |±30 mV|, and high EE% ($>$ 50%). Both FAV-NIO and FAV-CS-0.5 showed a high interaction with mucin. BBB-PAMPA results showed that FAV-CS-0.5 has significantly higher permeability than FAV-NIO and initial FAV. FAV-CS-0.5 showed a higher release rate in comparison to FAV-NIO and initial FAV. The *ex vivo* results showed that FAV diffusion from FAV-NIO and FAV-CS-0.5 through the human nasal mucosa was higher than initial FAV. Finally, the biopharmaceutical parameters were significantly improved in both FAV-NIO and FAV-CS-0.5 compared to initial FAV.

Conclusion: Utilising niosomes and chitosomes to deliver FAV through intranasal administration could be a promising approach to improve its low bioavailability and therapeutic effect.

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Author contributions: Conceptualization, Maryana Salamah; Methodology, Maryana Salamah; Software, Maryana Salamah; Validation, Maryana Salamah; Formal analysis, Maryana Salamah; Investigation, Maryana Salamah; Writing - original draft, Maryana Salamah; Writing - review and editing, Maryana Salamah; Visualization, Maryana Salamah;



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Sciforum-211246: Asymmetric liposomes prepared with a simple cyclodextrin-lipid complex method to improve performance of vesicles beyond conventional liposomes

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Developing liposomes delivery system via membrane asymmetry can offer more advantages to liposomal research. This research aims to produce asymmetric liposomes via a simpler cyclodextrin-lipid complexation and exchange method compared to that first produced by E. London and co-workers. Our procedures include formulating the cyclodextrin, CD, complex with the lipid (e.g. DOTAP) i.e donner. Large unilamellar vesicles (LUV, acceptor) formulated via thin film hydration method, where the required lipids, 4mM, were dissolved in chloroform, a thin film was formed. HEPES buffer hydrated thin film. Finally, equal volumes of the cyclodextrin-lipid complex and acceptor LUV dispersion were mixed to allow lipid exchange. Then asymmetric liposomes were separated by centrifugation. Fluorescence quenching and zetapotential, ZP, methods confirmed liposomes' asymmetry. Liposomes were analysed using size and ZP analysis, UV/VIS spectrophotometry to calculate entrapment efficiency (EE), and pH gradient with Bromocresol green, BCG, used to qualitatively confirm EE. Optimised formulation containing POPC in outer leaflet and POPC (15%), DOTAP (45%), and cholesterol (40%) was used to entrap salmon sperm DNA. The EE was determined using nanodrop lite, where 6µl of DNA (10mg/ml) was added to 2mM of asymmetric liposomes at a ratio of 19.4:1 liposome to DNA. Results of ZP established the asymmetry of liposomes as when neutral lipid POPC has been used as an acceptor LUV (inner) and DOTAP was formulated as a CD-lipid complex donor (outer layer), ZP of liposomes increased from -7.1 to 33.9mV and the vice versa when the CD-lipid complex formed with POPC to be outer layer led to reducing the ZP from 23.5 to 16.2mV. Optimised formula exhibited good asymmetric membrane integrity and EE via using BCG as a visual indicator and good encapsulation of DNA, with EE of 92.5%, size of 198.48nm and ZP of 26.4mV.



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Sciforum-211259: Phenylboronic Acid-Functionalized, Naringin-Loaded Zinc Oxide Nanocarriers: A pH-Responsive, Actively-Targeted Nanocarrier for Breast Cancer Therapy

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Conventional breast cancer chemotherapy is limited by poor tumour selectivity and systemic toxicity, motivating stimuli-responsive, actively-targeted nanocarriers. Here, naringin (NG)-loaded zinc oxide nanoparticles (NG-ZnONPs) were synthesised via alkaline co-precipitation using a Quality-by-Design approach with a Box-Behnken Design, then surface-functionalised by silanization and 4-formylphenylboronic acid conjugation to form a pH-labile Schiff-base linkage (PBA-NG-ZnONPs) for sialic-acid-receptor-mediated active targeting. Surface plasmon resonance (UV-Vis, 356 nm) and the imine bond (FTIR, 1560 cm^{-1}) confirmed successful conjugation. XRD/SAED confirmed a hexagonal wurtzite structure (20.1–20.3 nm), while TEM revealed anisotropic, organically-capped nanorods (73.0–120 × 19.5–30.8 nm). PBA-NG-ZnONPs showed a hydrodynamic diameter of 341.9 nm (PDI 0.386, ZP -9.4 mV), with 91.14% entrapment efficiency for NG-ZnONPs and 89.69% DEE and 36.51% DLC for PBA-NG-ZnONPs. Dialysis studies confirmed pH-dependent, acid-triggered release (41.40% at pH 5.0, 21.76% at pH 6.0, 3.07% at pH 7.4; 48 h). NG-ZnONPs showed potent antioxidant activity (DPPH IC_{50} = 236.88 µg/mL; ABTS IC_{50} = 229.06 µg/mL), while PBA-NG-ZnONPs showed nearly 3-fold greater cytotoxicity against MCF-7 cells (IC_{50} = 56.51 µg/mL) than free naringin, unmodified ZnONPs, or non-functionalized NG-ZnONPs. These results suggest that PBA-NG-ZnONPs are an efficient, stimuli-sensitive drug-delivery platform with promise for site-specific cancer treatment, combining two distinct approaches: sialic acid receptor-mediated cellular targeting and endosomal pH-triggered drug release.

Author contributions: Conceptualization, Shailendra Shivaji Gurav; Methodology, Harshita Shet; Formal analysis, Shailendra Shivaji Gurav; Investigation, Shailendra Shivaji Gurav and Harshita Shet; Resources, Harshita Shet; Data curation, Harshita Shet; Writing - original draft, Harshita Shet; Writing - review and editing, Shailendra Shivaji Gurav; Supervision, Shailendra Shivaji Gurav; Project administration, Shailendra Shivaji Gurav;



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Sciforum-211260: Green Nanotechnology with *Curcuma zedoaria*: Phytochemical Characterization and *In-vitro* Antioxidant Activity of Biosynthesized Zinc Oxide Nanoparticles

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Curcuma zedoaria is a medicinal plant rich in secondary metabolites with reported antioxidant and pharmacological properties. However, the potential biomedical application of plant-derived bioactive compounds may be constrained by challenges associated with their delivery and bioavailability. Plant-mediated nanoparticle synthesis offers an approach for developing nanomaterials that warrant further investigation as potential delivery platforms for bioactive constituents. This study evaluated the phytochemical composition of an ethanolic extract of *C. zedoaria*, the acute toxicity of the test preparation, and the physicochemical characteristics and in vitro antioxidant activity of *C. zedoaria*-mediated zinc oxide nanoparticles (ZnO-NPs). Preliminary quantitative phytochemical screening was performed on the extract, while ZnO-NPs were prepared using the green synthesis precipitation-based method involving the freshly prepared aqueous plant extract. Acute toxicity was evaluated in experimental animals following oral administration. Nanoparticle crystallinity and elemental composition were assessed using X-ray diffraction (XRD) and energy-dispersive X-ray (EDX) spectroscopy, respectively. Antioxidant activity was investigated using the 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical-scavenging and ferric reducing antioxidant power (FRAP) assays. The extract contained several phytochemical groups, with alkaloids and terpenoids among the most abundant constituents (17.05 ± 0.19 and 17.05 ± 0.01 mg/mL, respectively), followed by phenols (16.82 ± 0.02 mg/mL) and flavonoids (13.30 ± 0.13 mg/mL). No mortality or observable adverse reactions were recorded up to 5000 mg/kg body weight under the conditions of the oral acute toxicity assessment. XRD analysis confirmed crystalline ZnO-NPs, with an estimated average crystallite size of 12.39 nm, while EDX revealed prominent zinc and oxygen signals. The ZnO-NPs exhibited concentration-dependent DPPH radical-scavenging activity, reaching 67.47% inhibition, with a reported IC_{50} of 0.10 µg/mL. FRAP activity also increased with concentration, reaching 1.21 ± 0.00 mg ascorbic acid equivalents (AAE) at 250 µg/mL. These findings demonstrate the phytochemical richness of *C. zedoaria* and the potential of its extract as a biological component in the preparation of crystalline ZnO-NPs with measurable *in-vitro* antioxidant activity. The findings provide a basis for further investigation of their safety, formulation characteristics, bioavailability, and release behaviour before determining their suitability for specific biomedical applications.

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Sciforum-211298: Electrostatically stabilized anti-VEGFA siRNA—peptide polyplexes for anti-angiogenic therapy of endometriosis

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Endometriosis (EM) is a benign gynecological condition characterized by the aberrant proliferation of endometrial cells outside the uterine cavity. This pathological cell growth, accompanied by neoangiogenesis, contributes to the formation of EM lesions. Current pharmacological interventions for EM are often associated with adverse side effects, underscoring the necessity for alternative therapeutic strategies to improve disease management. Small interfering RNA (siRNA) therapeutics have emerged as a versatile pharmaceutical platform for treating a range of diseases; however, their clinical application is limited primarily by challenges related to effective delivery. Peptide-based nanoparticles designed for siRNA delivery offer a promising solution by enabling receptor-specific targeting and mitigating issues related to excessive positive charge. In this study, we engineered ternary polyplexes comprising anti-VEGFA siRNA, a cationic arginine-rich polymer, and an anionic glutamate-rich polymer functionalized with a cyclic RGD (cRGD) peptide to target $\alpha V\beta 3$ integrins. These polyplexes were subjected to physicochemical characterization, and their cytotoxicity and gene silencing efficacy against a GFP reporter were evaluated in vitro. The anti-angiogenic potential of the formulations was further assessed in vivo using a surgically induced EM model in female Wistar rats. Treatment with cRGD-decorated, anti-VEGFA siRNA-loaded peptide-based nanoparticles resulted in a significant reduction in the volume of EM lesions, accompanied by decreased VEGFA mRNA expression and diminished surface expression of the endothelial marker CD34, relative to control nanoparticles lacking the targeting ligand. Collectively, these findings demonstrate that anionic nanoparticles targeting $\alpha V\beta 3$ integrins can effectively suppress angiogenesis within EM lesions, highlighting their potential as promising candidates for the development of anti-angiogenic therapies in endometriosis.

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Sciforum-211460: Development of a three-layered keratin-based nanofibrous scaffold as an *in vitro* model of the human nail barrier

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Nail infections, particularly onychomycosis, affect millions of people worldwide, reducing quality of life. Therapeutic efficacy remains limited by the nail plate's dense keratinised structure, which restricts topical drug permeation. Current *in vitro* models based on human nails or animal hooves face structural variability, ethical and availability constraints, while synthetic alternatives fail to replicate the nail's architecture and biochemical composition, limiting their predictive value.

This study reports the development of a multilayer biomimetic ungual model based on a nanofibrous scaffold produced by sequential electrospinning, combining synthetic polymers with keratin extracted from human hair to mimic the three layers that constitute the nail plate. A biomimetic lipid layer was subsequently deposited to reproduce the protein–lipid interface governing transungual transport.

Structural characterisation confirmed a stratified architecture with distinct fibre morphologies across layers, consistent with native nail organisation. Functional validation was performed by *in vitro* permeation assays in Franz diffusion cells, using caffeine (hydrophilic) and terbinafine (lipophilic) as model compounds. The multilayer model significantly reduced caffeine flux ($J = 5.04 \pm 0.23$ μg/cm^2/h), approximately 2.3-fold lower than simpler nanofibrous structures, confirming its barrier function. Conversely, terbinafine permeation increased ~2.7-fold, reflecting preferential affinity for the incorporated lipid domains.

These results indicate that the model reproduces key physiological features of the human nail, capturing compound-dependent selective permeation. This reproducible platform offers a promising alternative to current nail surrogates for transungual delivery research and provides a robust basis for ongoing work on developing an infected onychomycosis model for disease-state drug screening.

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Sciforum-211500: Apis mellifera Royal Jelly-derived Extracellular Vesicles (RJ-EVs) as Novel Anti-inflammatory Nanotherapeutics for Equine Metabolic Syndrome-Affected Adipose Stem Cells

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Equine metabolic syndrome (EMS) is a multifactorial endocrine disorder characterized by insulin resistance, regional adiposity, and chronic low-grade inflammation, collectively driving functional impairment of adipose tissue-derived stem cells (EqASCs). Royal Jelly-derived extracellular vesicles (RJ-EVs) are emerging as bioactive nanoconstructs endowed with immunomodulatory and pro-regenerative properties; however, their potential in metabolic disease contexts remains largely unexplored. This study aimed to isolate and characterize RJ-EVs and to evaluate their cytocompatibility and immunomodulatory capacity in EMS-affected EqASCs *in vitro*.

RJ-EVs were isolated from raw Royal Jelly using the miRCURY Exosome Isolation Kit and characterized by scanning electron microscopy (SEM) and flow cytometry-based immunophenotyping targeting the surface markers CD9 and CD63, and, following bead permeabilization, the intraluminal marker Syntenin-1 and the cargo protein MRJP1. EqASCs isolated from healthy ($EqASC_{HE}$) and EMS-affected ($EqASC_{EMS}$) horses were treated with RJ-EVs at different doses for 24, 48, and 72 hours under serum free conditions. Cytocompatibility was assessed by MTS assay and Annexin V flow cytometry, and inflammatory profiling was performed by RT-qPCR and Western blot.

SEM confirmed a heterogeneous nanoscale vesicle population with spherical to ovoid morphology. Immunophenotyping validated CD63 and CD9 as EV surface markers, confirmed Syntenin-1 as an intraluminal EV marker, and identified MRJP1 as a candidate RJ-EV-associated cargo protein. RJ-EV treatment enhanced $EqASC_{EMS}$ viability in a dose and time dependent manner with no cytotoxic effects, and Annexin V analysis indicated a reduced apoptotic fraction, accompanied by downregulation of p53 and BAX and upregulation of BCL-2. At the inflammatory level, RJ-EVs suppressed the pro-inflammatory mediators IL-1β and MCP-1, with concurrent changes in IL-4 and IL-6 expression at both transcriptional and protein levels.

RJ-EVs exert cytoprotective and immunomodulatory effects on $EqASC_{EMS}$ *in vitro*, supporting a rationale for their further investigation as a naturally-derived nanotherapeutic candidate in metabolic disease.

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Sciforum-211598: From Sustainable Nanotechnology to Ovarian Cancer Theranostics: A Co-Creation Approach

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Ovarian cancer remains among the deadliest gynecological diseases, highlighting the needfor innovative therapeutic strategies that combine enhanced treatment efficacy withsustainable and socially inclusive approaches. This preliminary study investigateddoxorubicin association with graphene oxide quantum dots and its release under differentpH conditions.

As a preliminary step, graphene oxide quantum dots were synthesized through aconventional chemical route and evaluated as nanocarriers for the anticancer drugdoxorubicin. The nanoplatform was characterized by scanning electron microscopy,dynamic light scattering, UV–Vis and fluorescence spectroscopy, and ATR-FTIR, providinginsights into its morphological, physicochemical, surface, and optical properties. Theresulting nanoconjugates exhibited a hydrodynamic size of 108 ± 49 nm and greenfluorescence, with a quantum yield of 19.69%. Drug release kinetics were evaluated bydialysis at pH 5.5 and 7.4, at 37 ± 1 °C, over 24 h. The nanoconjugates reached 63.2% of themaximum drug release after 3.36 h at pH 5.5, compared with 5.52 h at pH 7.4,demonstrating pH-dependent drug release. These findings support the potential of thenanoconjugates for tumor microenvironment-responsive drug delivery, while their intrinsicfluorescence further supports their potential for bioimaging and theranostic applications.

Building on these preliminary findings, future work will investigate agricultural residues asalternative carbon precursors and develop a framework for community participation andco-creation.

Overall, this study supports the potential of these nanoconjugates as a pH-responsivenanotheranostic platform combining drug delivery and intrinsic fluorescence for potentialcancer applications, while providing a basis for future integration of sustainablenanomaterial production and community co-creation.

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Sciforum-211603: Microwave-Assisted Synthesis and AFM Characterization of Chitin- and Chitosan-Derived Carbon Quantum Dots for Biomedical Applications

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Effective delivery of therapeutic agents to the central nervous system remains challenging because of the restrictive nature of the blood–brain barrier. Intranasal administration offers a promising non-invasive route for nose-to-brain drug delivery. Chitosan is a biocompatible, biodegradable, and mucoadhesive biopolymer, while chitin is an abundant natural precursor with potential for producing carbon-based nanomaterials. In this study, chitosan- and chitin-derived carbon quantum dots (CQDs) were synthesized using a simple microwave-assisted bottom-up method. The precursor material was dispersed as a heterogeneous slurry in methanol for three hours on a magnetic stirrer, separated by centrifugation, washed with MilliQ water, filtered, and subjected to microwave treatment reaching temperatures higher than 65C. To ensure safety for intranasal application, residual toxic solvents were completely removed via solvent evaporation. The resulting nanoparticles were recovered in ethanol and in water and deposited on freshly cleaved mica for atomic force microscopy characterization. AFM imaging revealed relatively homogeneous nanoparticles with dimensions ranging from approximately 3 to 6 nm. These findings demonstrate that a microwave-assisted procedure can produce nanoscale carbon dots from chitin and chitosan precursors. Their small size, together with the biocompatible origin and potential surface functionality of the precursor materials, supports their further investigation as nanocarriers, fluorescent imaging agents, and biosensing platforms. Due to early stages of protocol development, additional studies will evaluate their chemical composition, fluorescence properties, colloidal stability, drug-loading capacity, prioritizing cytocompatibility, and interactions with biological interfaces relevant to intranasal delivery.

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Sciforum-211618: Development of Nanostructured Lipid Vesicles Encapsulating *Adenium obesum* and Coenzyme Q10: A Combinatorial Preventive Approach for the Management of Neurological Disorders

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Background: Cognitive impairment is prevalent in disorders and aging, and is worsened by oxidative stress, neuroinflammation, and cholinergic dysfunction. Aluminum chloride ($AlCl_3$)-induced neurotoxicity models exhibit cognitive deficits and Alzheimer's disease-like pathology. *Adenium obesum* and Coenzyme Q10 (CoQ10) may provide neuroprotective benefits. **Objective:** This study aimed to investigate the neuroprotective effects of *Adenium obesum* and CoQ10, administered individually and in combination, against $AlCl_3$-induced cognitive impairment in rats. This study also evaluated the potential of Nanostructured Lipid Vesicles (NLVs) to enhance the bioavailability and brain delivery of these therapeutic agents. **Methods:** Cognitive impairment was induced in rats using aluminum chloride ($AlCl_3$). Thereafter, the rats in the treatment groups were treated with nanostructured lipid formulations in suitable dose (160 mg/kg body weight) of *adenium obesum* extract and CoQ10 (1.5 mg/kg body weight). Behavioral assessments, including the Morris Water Maze (MWM) and Elevated Plus Maze (EPM), were performed to evaluate learning and memory functions. Biochemical analyses were conducted to determine the acetylcholinesterase (AChE) activity, oxidative stress markers, and antioxidant enzyme levels. The NLC formulation was developed to improve stability, bioavailability, and targeted brain delivery of therapeutic compounds. **Results:** Treatment with *adenium obesum* extract and CoQ10 significantly improved cognitive performance and attenuated $AlCl_3$-induced memory deficits in rats compared to the disease control group. The combination therapy delivered through NLVs exhibited superior neuroprotective activity, as evidenced by enhanced behavioral outcomes, reduced acetylcholinesterase (AChE) activity, decreased oxidative stress, and improved antioxidant defense mechanisms. Furthermore, the NLV-based formulation improved drug delivery efficiency, contributing to enhanced therapeutic efficacy.

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Sciforum-212963: Vinpocetine-Loaded Liposomes for Nose-to-Brain Delivery: Impact of Surface Charge and Drug Loading

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Vinpocetine is a lipophilic neuroprotective compound with poor aqueous solubility, which may restrict its therapeutic potential in neurodegenerative disorders. Nose-to-brain delivery offers a promising route to improve drug transport to the central nervous system. Liposomal nanocarriers may facilitate the incorporation of lipophilic drugs into an aqueous dispersion and improve their formulation characteristics. Building on our previous work on oppositely charged liposomal systems, this study aimed to develop and characterise surface-charged vinpocetine-loaded liposomes for potential nose-to-brain application.Vinpocetine-loadedformulationsphosphatidylcholine and cholesterol, modified with stearylamine (SA) or dicetyl phosphate (DCP) to obtain positively or negatively charged vesicles, respectively.Vinpocetine-to-phosphatidylcholine weight ratios of 1:8, 1:4, and 1:2 were investigated.Liposomes were prepared by thin-film hydration and characterised for particle size, polydispersity index (PDI), zeta potential, and encapsulation efficiency. Thermal and spectroscopic analyses were performed to investigate drug incorporation, while in vitro release studies were conducted to assess formulation performance.Vinpocetine-loaded formulations showed mean particle sizes ranging from 115 to 224 nm, with PdI values of 0.16-0.40. DCP-containing formulations were generally smaller and showed negative zeta potentials (-36.8 to -28.1 mV), whereas SA-containing formulations showed positive zeta potentials (+9.8 to +26.7 mV). Thermal and spectroscopic analyses indicated composition-dependent changes in lipid bilayer characteristics and supported vinpocetine incorporation. In vitro release was influenced by surface-charge modifier and vinpocetine loading, with lower drug loading generally associated with faster release.Overall, the findings demonstrate that lipid composition, surface charge, and vinpocetine loading influenced the physicochemical, structural, and in vitro performance of the liposomes. These findings support further optimisation and biological evaluation of the formulations for their intended nose-to-brain application.



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Sciforum-213800: Buffalo Milk-Derived Extracellular Vesicles Loaded in a Hyaluronic Acid Spray: A Novel Nano-Formulation for Skin Barrier Restoration in Psoriasis

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Psoriasis is a chronic inflammatory skin disorder characterized by dysregulation of the immune response, particularly involving activation of the IL-23/Th17 signalling pathway, together with increased oxidative stress and impairment of skin barrier function. These pathogenic mechanisms contribute to persistent inflammation, keratinocyte hyperproliferation, and tissue damage, highlighting the need for innovative therapeutic strategies capable of restoring cutaneous homeostasis. In this study, extracellular vesicles derived from buffalo milk (BM-EVs) were investigated as a natural bioactive platform for skin protection and regeneration. BM-EVs were isolated and extensively characterized, revealing physicochemical properties suitable for topical applications. Metabolomic profiling demonstrated that these vesicles carry a diverse cargo enriched in vitamins and antioxidant-related metabolites, suggesting a potential role in modulating oxidative stress and supporting cellular functions involved in skin repair. To enhance topical delivery and improve retention on the skin surface, BM-EVs were incorporated into a spray formulation based on high-molecular-weight hyaluronic acid (HMW-HA). The resulting formulation exhibited rheological characteristics favourable for atomization and uniform distribution, while also benefiting from the well-known moisturizing, protective, and barrier-supporting properties of hyaluronic acid. The biological activity of BM-EVs was evaluated in human fibroblasts under oxidative stress conditions. The vesicles showed excellent biocompatibility and effectively protected cells from oxidative damage by reducing intracellular reactive oxygen species and limiting lipid peroxidation. These findings suggest that BM-EVs can contribute to the maintenance of redox balance and cellular integrity. BM-EV-loaded HMW-HA spray represents a promising, non-invasive nanomedicine approach for supporting skin homeostasis and mitigating oxidative damage and barrier dysfunction associated with psoriasis.

Author contributions: Conceptualization, Anna Valentino; Methodology, Fabrizia Sepe; Validation, Fabrizia Sepe and Raffaele Conte; Formal analysis, Raffaele Conte and Orsolina Petillo; Investigation, Fabrizia Sepe; Data curation, Raffaele Conte; Writing - review and editing, Anna Valentino; Supervision, Anna Calarco; Project administration, Orsolina Petillo; Funding acquisition, Anna Calarco;



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Session 9. Formulation, Drug Delivery, and Controlled Release

Sciforum-184693: Development and evaluation of cricket (*Teleogryllus occipitalis*) oil as a natural lipid base for suppository formulation

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Background & Objectives: Most key raw materials used in pharmaceutical manufacturing in the Philippines are imported, highlighting the need to explore locally available alternatives (Reyes & Tabuga, 2020). Cricket oil has gained attention as a potential natural lipid source because of its reported antioxidant, anti-inflammatory, and protective biological activities associated with phenolic compounds and phytosterols (Murugu et al., 2024). Although its applications in skincare and food industries have been described, its pharmaceutical use remains limited. This study aimed to extract and characterize Teleogryllus occipitalis oil and evaluate its potential as a natural lipid base for suppository formulation.

Methods: *Teleogryllus occipitalis* oil was extracted through pulverization, hexane maceration, vacuum filtration, rotary evaporation, bentonite purification, centrifugation, and decantation. The extracted oil was characterized using refractive index determination and FTIR-ATR analysis. Preliminary safety was assessed through the HET-CAM assay and brine shrimp lethality test. Three paracetamol suppository formulations containing cricket oil and beeswax were prepared, and their melting point and in vitro drug release were evaluated.

Results & Discussion: A total of 145.03 g crude oil was obtained from 608.85 g dried cricket sample, giving a 23.82% yield, which was higher than the 12.39% reported by Ngampeerapong et al. (2024). The oil had a mean refractive index of 1.4618 ± 0.0008, close to values reported for other cricket oils. FTIR-ATR analysis showed characteristic lipid absorption bands. In the HET-CAM assay, *T. occipitalis* oil was classified as non-irritating, while the brine shrimp lethality test showed only 10% mortality at 100 ppm, suggesting low preliminary toxicity. The oil was successfully formulated with beeswax into solid suppositories. Among the formulations, F2 showed the lowest mean melting point and the most consistent upward drug release pattern.



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Sciforum-204076: Development of Trazodone HCl Prolonged-Release Tablets: Formulation Optimization and Dissolution Studies

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Abstract

The present study aimed to develop and optimize prolonged-release tablets of Trazodone HCl using hydrophilic hydroxypropyl methylcellulose (HPMC) polymers of different viscosity grades and concentrations to achieve controlled drug release over 24 hours. Tablets were prepared by the direct compression method using HPMC K4M, HPMC K15M, and HPMC K100M at varying concentrations, followed by evaluation of assay and in vitro dissolution. Drug release studies were performed using USP Apparatus II in 0.1 N HCl for the first hour and phosphate buffer (pH 6.0) thereafter. The results demonstrated that both polymer viscosity and concentration significantly influenced the release profile. Formulations containing HPMC K4M and HPMC K15M exhibited rapid drug release. They failed to control the initial burst effect, while a low concentration of HPMC K100M was insufficient to establish an effective matrix. Increasing the concentration of HPMC K100M improved release control, with an optimized batch containing 25% w/w HPMC K100M providing the most desirable dissolution profile, achieving 26.68%, 48.81%, 82.47%, and 100.42% cumulative drug release at 1, 6, 12, and 24 hours, respectively. Reproducibility studies confirmed consistent performance of the optimized formulation. Overall, the optimized batch was identified as the optimal formulation and represents a promising prolonged-release system suitable for further stability evaluation, process scale-up, and pharmaceutical development.



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Sciforum-205493: Optimising Pharmaceutical Formulations in Resource-Limited Settings: A Hybrid Deep Learning Approach for Sustained-Release Tablets

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Introduction: Manufacturers in LMICs meet less than 20% of the demand for medical devices. Formulations of sustained-release tablets by means of design of experiments require 50-100 (costly) trials ($10k-15k per trial). Existing machine learning approaches (FormulationNet and PharmaML) depend on large proprietary datasets and GPU training. We intended to develop a CPU-based approach capable of predicting excipient ratios with a macro-average $R^2 \geq 0.90$.

Methods: A literature review yielded 151 formulations. Training was augmented with Gaussian perturbation and linear interpolation to 5,440 training samples. The test set (20%) was not augmented. A residual attention CNN was used to predict the ratios of polymer, binder, diluent, lubricant, and glidant. The ratio components with single-model R^2 below 0.85 were supplemented with a shallow ensemble MLP (three models, mean blend). A Streamlit app (DeepPharm®) was used for the CPU-only inference.

Results: CNN provided $R^2 = 0.933$ and RMSE = 0.049. The ensemble boost increased the macro-average R^2 to 0.941 (RMSE 0.044), with component-specific improvements for binder_ratio (0.812 to 0.877), lubricant_ratio (0.803 to 0.874), and glidant_ratio (0.798 to 0.871). SHAP analysis revealed that the fraction of polymer (|SHAP| = 0.42), kinetic R^2 (0.38), and API logP (0.31) were the three main predictors. The average latency of the end-to-end model on an Intel i5-10400 CPU was 420 ms (SD 35 ms).

Discussion: Based on the results, we expect a potential saving of ≥80% of experimental iterations and development timelines, from months to weeks (prospective validation is pending).



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Sciforum-207642: Development of a Pre-Measured Furosemide Oral Granules Kit for Paediatric Heart Failure in Sub-Saharan Africa Using a Quality-by-Design Approach

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Introduction: In Sub-Saharan Africa, paediatric heart failure therapy often relies on manual compounding of adult furosemide tablets, which may introduce dosing inaccuracies and stability concerns from aqueous hydrolysis and photodegradation in tropical climates. This study aimed to develop a pre-dosed furosemide oral granules kit using Quality-by-Design (QbD) to achieve content uniformity, chemical stability, and predictable reconstitution, supporting accurate dosing without cold-chain requirements.

Methodology: Pre-formulation studies and risk assessment (Ishikawa/FMEA) identified critical quality attributes, content uniformity, dissolution, and stability. A wet-granulation prototype (FOG-01) was optimised. Flow properties, moisture content, dispersion time, reconstitution time, and homogeneity were evaluated against predefined criteria. Accelerated stability was assessed over 4 weeks (40 °C ± 2 °C) and in-use stability of the reconstituted suspension at 25–30 °C and 2–8 °C under controlled laboratory conditions.

Results: Optimised granules exhibited good flow (Carr's index 17.5%), rapid dispersion (53 s), and homogeneity (USP acceptance value 4.8). Four-week accelerated stability showed 96.8% potency, 0.58% total impurities (limits 90–110%, ≤5%), and dissolution ≥89.5% at 15 min (≥80%). Reconstituted suspension potency remained acceptable for 7 days at room temperature and 14 days refrigerated. Preliminary lab-scale cost was estimated at USD 3.00–4.00 per kit.

Conclusions: The QbD-derived granule kit met the predefined quality targets, providing a potential alternative to manual compounding. Key limitations include evaluation of a single batch, short-term accelerated stability, and laboratory-based in-use testing; long-term real-time stability in Zone IVb, multi-batch validation, clinical studies, and caregiver usability assessments are necessary before widespread implementation. The preliminary cost projection requires manufacturing-scale verification.

Author contributions: Conceptualization, Yvonne Mhakayakora; Investigation, Yvonne Mhakayakora; Data curation, Yvonne Mhakayakora; Writing - original draft, Yvonne Mhakayakora; Writing - review and editing, Humphrey Masimba Makumbirofa; Supervision, Humphrey Masimba Makumbirofa;



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Sciforum-207711: Preparation and Preliminary Evaluation of a Dissolving Microneedles Delivery System Based on Living Chlamydomonas reinhardtii

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Background: Microalgae offer unique advantages in biomedicine due to their inherent biocompatibility, *in situ* photosynthetic oxygenation, and autonomous motility. **Delivering them live and intact into subcutaneous tissue is crucial to actively ameliorate hypoxic lesion microenvironments and enhance tissue penetration.** However, this efficient delivery is primarily hindered by the stratum corneum barrier. This study developed a novel composite platform integrating the biological functions of living microalgae with the transdermal delivery capabilities of dissolving microneedles (DMNs). **Methods:** Bioactive Chlamydomonas reinhardtii was cultured in TAP medium under a 16h:8h light-dark cycle. Using hyaluronic acid and polyvinylpyrrolidone (PVP K90) as the matrix, algae-loaded dMN arrays were fabricated via an optimized vacuum infiltration-centrifugation method. Array morphology, mechanical strength, and penetration capacity were evaluated using an *in vitro* Parafilm puncture model. **Results:** The fabrication process proved highly stable, yielding defect-free, regularly arranged conical dMN arrays. Mechanical testing demonstrated consistent strength, with the needles reliably penetrating three layers of Parafilm across multiple trials. The formulation successfully encapsulated the microalgae, preserved their viability, and exhibited the capacity to pierce the stratum corneum before rapidly dissolving in interstitial fluid to release the living cells. **Conclusions:** By encapsulating 36h-cultured microalgae within an optimized 400 mg/mL hyaluronic acid matrix via -0.07MPa vacuum and 4000 rpm centrifugation, this composite system achieved consistent penetration of a 3-layer simulated stratum corneum barrier under 2-minute compression. This "living-material" platform offers an innovative strategy for macromolecular or cell-level drug delivery and ameliorating hypoxic microenvironments at lesion sites, highlighting significant potential for clinical translation.



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Sciforum-208322: Phytosomal Based Delivery of Ellagic Acid: Formulation of an Oral Reconstitutable Suspension and Anthelmintic Evaluation

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Background: Helminthic infections constitute a serious global health burden. Even though ellagic acid exhibits remarkable anthelmintic activity, its poor aqueous solubility and low oral bioavailability impede its widespread clinical utility.**Aim:** To formulate and characterize an ellagic acid phytosomal dry powder for oral suspension (DPOS) and evaluate its anthelmintic efficacy through *in vitro* and *in silico* approaches.**Methodology:** Ellagic acid phytosomes were prepared with soya lecithin via solvent evaporation and homogenized to formulate a DPOS matrix. Entrapment efficiency was quantified using UV-Vis spectrophotometry, and complexation was confirmed by FTIR spectroscopy. Surface morphology of isolated phytosomes was characterized by scanning electron microscopy (SEM). Following reconstitution, optical microscopy was employed for particle size determination alongside assessments of sedimentation volume, pH, viscosity, and redispersibility. Anthelmintic efficacy was evaluated against *Pheretima posthuma* with albendazole as a reference drug. *In silico* SwissADME screening assessed physicochemical properties and drug-likeness, while molecular docking against the helminth tubulin receptor (PDB: 1SA0) determined binding affinities.**Results:** Scanning electron microscopy of isolated phytosomes revealed discrete micro-particulates ranging from 1.24 to 9.98 µm, with an entrapment efficiency of 85.24%. Upon reconstitution, the DPOS demonstrated a mean particle size of 11.15 µm, rapid redispersibility, and high physical stability (F = 0.92 +/- 0.02). Although conventional *in vitro* dissolution was unfeasible due to infrastructural limitations, enhanced wetting, dispersibility, and bio-uptake of the phospholipid matrix were corroborated biologically: the 100 mg/mL phytosomal suspension induced earthworm paralysis (34.00 +/- 2.18 min) and death (59.25 +/- 4.91 min) comparable to albendazole (33.28 +/- 1.17 min) and (57.90 +/- 4.31 min, respectively). *In silico* profiling confirmed the favorable drug-likeness of ellagic acid, and molecular docking demonstrated superior binding affinity to tubulin (-8.654 kcal/mol) relative to albendazole (-6.526 kcal/mol).

Author contributions: Conceptualization, Vasanthi A V; Methodology, Medha Gayatri Bhatiprollu and Kiranmai Kothapally; Software, Medha Gayatri Bhatiprollu; Validation, Medha Gayatri Bhatiprollu; Investigation, Komal Gaikwad; Resources, Komal Gaikwad and Kiranmai Kothapally; Data curation, Vasanthi A V; Writing - original draft, Vasanthi A V; Writing - review and editing, Vasanthi A V;



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Sciforum-208331: Non-Additive Solubility Enhancement in Multicomponent Drug–Cyclodextrin–L-Arginine Formulations

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Poor aqueous solubility remains a major limitation in the formulation of many active pharmaceutical ingredients. Cyclodextrins and amino acids can enhance apparent drug solubility through coupled effects involving ionization, inclusion complexation, multicomponent association, and solid–liquid partitioning. When these processes operate simultaneously, the resulting formulation response may become non-additive.

A thermodynamic equilibrium approach was applied to multicomponent systems containing repaglinide, sulfadiazine, cefixime, and meloxicam as representative active pharmaceutical ingredients and L-arginine as the amino acid component. The model accounts for drug protonation, binary drug–cyclodextrin complexation, drug–arginine interactions, ternary association, and precipitation of the free drug over selected pH and composition ranges. Hydroxypropyl-β-cyclodextrin (HPβCD) was included in the quantitatively validated repaglinide system.

Apparent drug solubility and solid-phase fractions were calculated for binary and ternary formulations. Non-additive enhancement was evaluated by comparing the ternary response with the corresponding drug–cyclodextrin system under identical conditions. The calculations show that the contribution of L-arginine is strongly pH-dependent and becomes most pronounced within restricted regions where favorable drug ionization, complex formation, and solid–liquid partitioning occur simultaneously. The largest enhancement is therefore associated with shifts in the coupled equilibrium network rather than with an independent contribution of a single excipient.

Quantitative comparison with published phase-solubility data for the **repaglinide–HPβCD–L-arginine** system supports the numerical consistency of the approach, while the other drug systems illustrate its predictive applicability. The results show that non-additive solubility enhancement can be interpreted as an emergent response of coupled equilibria and provide a thermodynamic basis for identifying favorable pH and excipient conditions in multicomponent pharmaceutical formulations.

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Sciforum-209365: Route-dependent astaxanthin delivery modulates granulocyte mitochondrial stress responses

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Astaxanthin is a potent natural lipophilic antioxidant with mitochondrial protective and anti-inflammatory properties. Its oral bioavailability is limited by poor aqueous solubility and first-pass metabolism. Alternative delivery routes may alter systemic and cellular availability. We aimed to compare the effects of sublingual, transdermal, and oral astaxanthin administration on granulocyte functional parameters associated with mitochondrial stress.

A prospective comparative study included 60 healthy volunteers divided into three groups (n=20 per group). Participants received astaxanthin for 30 days by sublingual administration (6 mg/day), transdermal administration (6 mg/day), or oral administration (12 mg/day). Granulocyte phenotypic profiling was performed at baseline and after one month using fluorescence microscopy. The assessed parameters included mitochondrial activity, protein metabolism, oxidative stress, oxygen and energy metabolism, and phagocytic activity. Mitochondrial activity was evaluated by the proportion of cells demonstrating mitochondrial accumulation, while oxidative stress was assessed based on spontaneous membrane damage. Oxygen metabolism was evaluated using the nitroblue tetrazolium (NST) test, and phagocytic activity using a latex particle assay.

Sublingual and transdermal administration produced greater improvements than oral administration. Mitochondrial activity increased by 25, 22, and 11 percentage points, respectively; protein metabolism by 22, 21, and 11 points; oxygen and energy metabolism by 13, 11, and 7 points; and phagocytic activity by 8, 6, and 4 points. Oxidative stress decreased by 21, 18, and 10 points, respectively. The greatest improvements in mitochondrial activity and reductions in oxidative stress were observed following sublingual and transdermal delivery.

The route of astaxanthin administration influences granulocyte mitochondrial and functional responses. Sublingual and transdermal delivery were associated with greater improvements in mitochondrial activity, metabolic function, oxygen metabolism, and phagocytic activity, together with reduced oxidative stress, compared with oral administration. Granulocyte phenotypic profiling may provide a functional approach for evaluating antioxidant delivery strategies and formulations aimed at mitochondrial protection.

Author contributions: Conceptualization, Darya Starodubtseva and Stanislav Panov; Methodology, Darya Starodubtseva and Stanislav Panov; Validation, Darya Starodubtseva and Stanislav Panov; Formal analysis, Darya Starodubtseva and Dayana Danayeva; Investigation, Darya Starodubtseva; Resources, Darya Starodubtseva and Stanislav Panov; Data curation, Darya Starodubtseva and Stanislav Panov; Writing - original draft, Darya Starodubtseva; Writing - review and editing, Dayana Danayeva; Supervision, Stanislav Panov; Project administration, Darya Starodubtseva and Stanislav Panov;



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Sciforum-209599: Optimization of a microneedle patch: composition and manufacturing process

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Introduction

The effective delivery of active substances through the skin is hindered by the limited permeability of the stratum corneum. Microneedles provide a minimally invasive approach to overcoming this barrier, enabling the transport of bioactive compounds to deeper layers of the epidermis. The aim of this study was to optimize the composition of the polymer matrix and the manufacturing parameters for the production of rapidly dissolving sodium hyaluronate-based microneedles using the freeze-thaw method.

Methods

Sodium hyaluronate solutions were prepared with the addition of inulin or trehalose. The preparation process was optimized by evaluating sonication for air-bubble removal and subsequent shaking of the filled molds. To achieve the desired needle sharpness, three freeze-thaw cycles were performed, varying the duration and method of thawing. The resulting structures were evaluated microscopically, as well as through betanin release assays, agar dissolution tests, and porcine skin penetration tests.

Results

Sonication effectively removed air bubbles from the sodium hyaluronate solutions and improved mold filling. Subsequently, shaking the filled molds for 60 minutes resulted in the best needle formation. Microneedles based on sodium hyaluronate and trehalose dissolved in agar within 30-40 s and penetrated porcine skin to a depth of approximately 350 μm.

Conclusions

The optimized method allowed for the reproducible production of stable patches with well-formed, sharp microneedles, showing rapid release of the model compound and indicating their potential in transdermal therapy.



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Sciforum-209952: Selection of a water-containing composition for 5-amino-4-(3-aminophenyl)-N-(tert-butyl)-2-(methylthio)thieno[2,3-d]pyrimidine-6-carboxamide (TP03), a luteinizing hormone receptor agonist: steroidogenic activity and bioavailability in male rats

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One of the areas of research in the search for effective stimulators of ovarian and testicular steroidogenesis is the development of low-molecular-weight allosteric agonists of the luteinizing hormone (LH) receptor, which offer several advantages over gonadotropins used in medicine. We previously developed 5-amino-4-(3-aminophenyl)-N-(tert-butyl)-2-(methylthio)thieno[2,3-d]pyrimidine-6-carboxamide (TP03), a steroidogenesis and ovulation stimulator. However, TP03, being a highly hydrophobic compound, is insoluble in water and is used as a solution in DMSO, which limits its practical applications. The aim of the study was to find the optimal water-containing composition for TP03, study the ability of TP03 in this composition to stimulate testosterone production and evaluate its bioavailability for the testes. Among the studied compositions, #2 – Solutol-HS15/PEG400/water 3:2:5, and #3 - DMSO/PEG400/Tween80/phosphate buffer 1:6:1:12 were suitable for TP03. In Composition #2, TP03, when administered orally (1.5, 3 and 5 mg/kg) and intraperitoneally (15 mg/kg) to male rats, stimulated testosterone production, and the hormone level in both cases increased after 30 minutes, which was not observed when TP03 was administered in DMSO. In Composition #3, TP03 (i.p., 15 mg/kg) resulted in a gradual increase in testosterone levels, reaching a maximum after 3 hours. This effect was superior to that observed with the DMSO solution. In Compositions #2 and #3, TP03 content in the blood and testes 3 hours after oral and intraperitoneal administration exceeded those observed with the DMSO solution, indicating higher bioavailability of TP03. Thus, optimal solubilization conditions for TP03 have been selected, which is important for the development of TP03-based drugs.

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Sciforum-209974: Development and Optimization of a Green Co-Processed Orange Peel Pectin–Flaxseed Mucilage Carrier for Solubility and Dissolution Enhancement of Candesartan Cilexetil

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Background

Candesartan cilexetil (CC) is a BCS Class II drug with low aqueous solubility, which is a large problem for dissolution and oral bioavailability. Sustainable plant-derived excipients commercially derived from agro-waste can be considered as an environmentally friendly alternative to the conventional synthetic solubility-enhancing systems.

Aim

To formulate and optimize orange peel pectin–flaxseed mucilage as a carrier for improvement of solubility and dissolution of CC.

Methods

Extraction of pectin and flaxseed mucilage was done using aqueous process and co-processing was carried out at 25:75, 50:50 and 75:25 ratio. The drug:carrier ratios were 1:1, 1:2 and 1:3 and the CC solid dispersions were prepared by the 3^2 factorial design. The practical yield, the drug content and the saturation solubility and in-vitro dissolution were tested. FTIR was used for the characterization of the optimized system.

Results

Pure CC was soluble in pH 7.4 phosphate buffer (0.48 mg/mL) and 0.1 N HCl (0.34 mg/mL). The solubility of F8 (1:3 drug:carrier; 50:50 pectin:mucilage) was the highest (0.86 and 1.24 mg/mL, respectively) which is about 2.53 and 2.58 fold increase with drug content of 99.0%, practical yield of 91.2% and drug release of 94% at 120 min.

Conclusion

The proposed approach involves agro-waste utilization, natural polymer engineering and factorial optimization, for developing a sustainable carrier for poorly soluble drugs. The optimized system is expected to offer an interesting green alternative to enhance the dissolution of CC.

Author contributions: Conceptualization, RAJAN NITINBHAI RANPARA; Methodology, RAJAN NITINBHAI RANPARA; Writing - original draft, RAJAN NITINBHAI RANPARA; Writing - review and editing, RAJAN NITINBHAI RANPARA; Supervision, RAJAN NITINBHAI RANPARA; Project administration, RAJAN NITINBHAI RANPARA;



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Sciforum-210347: Alginate hydrogels with reduced graphene oxide and condensed tannins: formulation programs polyphenol release for wound management

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Wound repair requires dressings that deliver bioactive agents in a sustained manner. To this end, borate-crosslinked alginate hydrogels were formulated to carry condensed tannins (TA) from *Pinus radiata* bark, with dopamine-reduced graphene oxide (rGO) as a network modulator. Nine formulations were prepared by combining three rGO and three TA levels (0, 4.5 and 9 wt%) and subjected to physicochemical characterization, swelling and release in PBS (pH 7.4; 37 °C), antioxidant and antibacterial activity, human fibroblast response and in vivo healing in pigs. The rGO content governed the release mechanism. At 4.5%, a compact, hydrophobic and markedly anionic surface layer was formed (-46.8 mV), with power-law exponents below 0.5, indicative of a sustained release controlled by TA diffusion through the pores of the gel. At 9%, network relaxation dominated: release was exhausted within 80 minutes, delivering only 26.4% of the loaded TA. TA determined the biological performance. It raised swelling to 60% of the weight, which favors exudate absorption, and provided antioxidant capacity (46 mg Trolox equivalents/100 g) and activity against *Escherichia coli*. Fibroblast viability reached 145% of the control, indicating that the material stimulates proliferation. In vivo, Alg/rGO9/TA9, the most heavily loaded formulation, closed the wound by day 21, suggesting that its rapid release concentrates antioxidant and antibacterial action in the early inflammatory phase. Overall, rGO loading makes it possible to program polyphenol release in bioactive dressings.



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Sciforum-210350: Influence of thermal treatment on doxycycline release from clinoptilolite-rich natural zeolite carriers

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Natural zeolites have attracted increasing interest as inorganic carriers for drug delivery because of their porous framework, ion-exchange properties, chemical stability, and broad availability. In this study, a clinoptilolite-rich natural zeolite of Romanian origin and samples thermally treated at 150, 200, and 250 °C were evaluated as carriers for doxycycline, with particular attention to the influence of thermal treatment on drug release under simulated physiological conditions. The untreated and thermally treated zeolites were loaded with doxycycline by adsorption from aqueous solution at an initial drug-to-carrier ratio of 200 mg/g, under controlled pH and continuous stirring at room temperature. The loaded zeolites were subsequently evaluated in simulated gastric fluid (pH 1.2) followed by simulated intestinal fluid (pH 6.8) at 37 °C. Doxycycline release was quantified by high-performance liquid chromatography (HPLC) at predetermined time intervals, and cumulative release was expressed relative to the amount of drug initially incorporated into each carrier. The release profiles showed that thermal treatment modified doxycycline–zeolite interactions, resulting in distinct differences in drug retention, release rate, and cumulative release among the investigated samples. These differences were dependent on treatment temperature, indicating that thermal modification can affect pore accessibility and the strength of drug–carrier interactions. The release data were further analyzed using Higuchi, Korsmeyer–Peppas, and first-order kinetic models to gain insight into the mechanisms governing doxycycline release from the zeolite matrix. Overall, the findings indicate that thermal treatment provides a straightforward means of modulating doxycycline release from clinoptilolite-based carriers and support the further development of natural zeolites as tunable inorganic platforms for controlled antibiotic delivery.

Author contributions: Conceptualization, Oana Cadar and Selin Şahin; Methodology, Oana Cadar, Anca Becze, Dorina Simedru and Alexandra Daniela Scurtu; Validation, Anca Becze; Formal analysis, Oana Cadar, Anca Becze, Dorina Simedru and Alexandra Daniela Scurtu; Investigation, Oana Cadar, Anca Becze, Dorina Simedru and Alexandra Daniela Scurtu; Writing - original draft, Oana Cadar; Writing - review and editing, Oana Cadar and Selin Şahin; Visualization, Selin Şahin; Supervision, Oana Cadar and Selin Şahin; Project administration, Oana Cadar and Selin Şahin;



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Sciforum-210426: Assessment of the Effect of an Organic Solvent on the Physicochemical Properties of Polymer Nanoparticles

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Polymer nanoparticles are promising drug delivery systems that enable drug encapsulation. Their stability and safety depend on synthesis conditions, particularly the choice of organic solvent. This study evaluated the stability of polylactide-co-glycolide nanoparticles for peptide “Ipamorelin” delivery, synthesized using ethyl acetate, acetone, and dimethyl sulfoxide (DMSO). Nanoparticles were prepared by nanoprecipitation using polyvinyl alcohol as a stabilizer. Particle physicochemical characteristics were measured by dynamic light scattering 1 hour after preparation and after one week. All samples remained within the target size range of 100–250 nm. Nanoparticles synthesized with ethyl acetate and DMSO demonstrated multimodal size distributions of 164/190 nm and 190/220 nm, respectively. The acetone-based sample initially exhibited a monomodal distribution with a peak at 190 nm; after one week, a secondary peak at 164 nm appeared, potentially indicating the onset of degradation. The zeta potential of all systems remained between -15 and -5 mV, suggesting overall physical stability. The exception was the ethyl acetate sample, for which the zeta potential shifted from -13 to -7 mV. Overall, the solvent did not significantly affect particle size distribution or structural stability. However, solvent toxicity remains an important consideration. Acetone and ethyl acetate are more hazardous than DMSO, limiting their suitability for pharmaceutical applications. Therefore, material safety should take priority over minor differences in nanoparticle physicochemical properties.

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Author contributions: Conceptualization, Aleksandr Andreevich Nazarov and Gleb Vladimirovich Petrov; Methodology, Aleksandr Andreevich Nazarov; Formal analysis, Aleksandr Andreevich Nazarov; Investigation, Aleksandr Andreevich Nazarov; Data curation, Gleb Vladimirovich Petrov; Writing - original draft, Aleksandr Andreevich Nazarov; Writing - review and editing, Aleksandr Andreevich Nazarov and Gleb Vladimirovich Petrov; Supervision, Gleb Vladimirovich Petrov;



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Sciforum-210479: Design and Characterization of Azithromycin-Loaded Pectin-Hyaluronic Acid Nano Hydrogel for the Treatment of Skin Infections

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Purpose: Skin infections remain a major clinical concern due to rising antimicrobial resistance and the poor skin penetration of conventional topical formulations. This study developed and characterised an azithromycin -loaded novasome-incorporated pectin-hyaluronic acid nano hydrogel formulation for localised drug delivery in skin infections, designed to enhance skin retention, penetration, and controlled drug release. Methods: Azithromycin-loaded novasomes (stearic acid, oleic acid, Span 80, cholesterol) were prepared by ethanol injection and optimised via a design-of-experiments for minimum particle size and maximum drug loading. Optimised novasomes were incorporated into a pectinhyaluronic acid-gellan gum hydrogel, cross-linked with tartaric acid, and evaluated for physicochemical properties, FTIR compatibility, sterility, in-vitro drug release, ex-vivo skin permeation, antibacterial efficacy, and in vivo wound healing in a S. aureus-infected rodent model with histopathological analysis. Results: Optimised novasomes showed a particle size of 118.7±39.7 nm and drug loading of 66.762±0.013%. The nano hydrogel exhibited skin-compatible pH (5.286±0.015), spreadability (75±0.577 g.cm/s), and viscosity (37,500±358.573 cP) with shear-thinning behaviour. FTIR confirmed no drug-excipient interaction. The nanogel showed sustained, controlled drug release and greater ex-vivo skin permeation than the marketed gel, with larger zones of inhibition against S. aureus. In-vivo, the nanogel produced faster wound contraction and near-complete healing by Day 15, with histopathology confirming enhanced reepithelialization, collagen deposition and fibroblast proliferation. Conclusion: The novasome-loaded nano hydrogel offers a promising controlled-release topical platform for effective azithromycin delivery in bacterial skin infections.



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Sciforum-210568: Exploring the Impact of Nanocarrier Composition in Thermo-responsive Hydrogels

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Personalized medicine increasingly requires drug delivery systems that can be adapted to specific therapeutic needs while maintaining formulation simplicity and reproducibility. In this context, thermoresponsive hydrogels are attractive because they combine injectability, *in situ* gel formation and sustained release of entrapped compounds. Their coupling with nanocarriers may further increase the versatility of these systems by modulating their physicochemical properties and drug release behavior.

Based on this, two thermoresponsive nanocomposite formulations were investigated in order to evaluate the influence of nanocarrier composition and surface properties.

Initially, poloxamer 407 (P407), one of the most widely investigated thermoresponsive copolymers for drug delivery, was combined with liposomes characterized by different lipid composition and surface properties. The inclusion of liposomes preserved the thermogelation and viscoelastic behaviour of hydrogels, whereas physical stability was strongly influenced by the vesicular composition and surface architecture, with charged and PEGylated systems showing greater stability than neutral formulations. These differences may reflect distinct liposome-matrix interactions, including hydrophobic interactions between P407 domains and lipid bilayers.

Successively, the same approach was applied to poloxamine 908 (P908), an X-shaped amphiphilic copolymer characterized by both temperature- and pH-responsive behaviour. P908 was combined with nanoparticles made up of poly(lactic-co-glycolic acid) (PLGA) or zein, stabilized with poloxamer 188 (P188) or sodium deoxycholate (SD). The polymer and stabilizer employed significantly modulated the main properties of P908 matrix. Zein nanoparticles prepared with different stabilizers promoted distinct effects on network strength, sol-gel transition and dissolution; in detail, SD-stabilized zein nanoparticles exerted the most pronounced changes in hydrogels, while the Zeta-potential of the colloidal systems affected their drug release, especially under acidic conditions.

These findings demonstrate that nanocarrier-matrix compatibility is a key factor of nanocomposite hydrogels, supporting the design of responsive local drug delivery systems tailored to different therapeutic needs.



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Sciforum-210569: Hydroxytyrosol-Loaded Zein Nanoparticles: A Versatile Formulation for Pharmaceutical and Nutraceutical Applications

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Hydroxytyrosol (Htyr) is one of the most bioactive phenolic compounds derived from olive by-products and is widely recognized for its antioxidant, anti-inflammatory and protective biological activities. Despite its relevance, its use in functional foods or nutraceutical formulations is hindered by poor stability, rapid metabolism and limited absorption. To address these issues, an eco-friendly nanoformulation was developed using zein (2 mg/mL), a GRAS corn protein, stabilized with sodium deoxycholate (SD, 1.25% w/v) and loaded with Htyr (0.2–2.0 mg/mL). Empty nanoparticles showed a mean diameter of approximately 100 nm, low polydispersity and a negative zeta potential (~ –30 mV). The addition of Htyr at 1.6 mg/mL produced nanosystems with an entrapment efficiency of ~60% (≈1.0 mg/mL retained) and a loading capacity of ~25%. FT-IR spectroscopy indicated that hydrogen bonding and electrostatic interactions were the main stabilizing forces within the formulation. The nanoparticles preserved their structural integrity after pasteurization (65 °C, 30 min), heating up to 95 °C and exposure to ionic strengths up to 150 mM NaCl. Simulated gastrointestinal assays confirmed effective protection of Htyr in gastric fluid (~7% release at pH 1.2 with pepsin) and a controlled release profile under intestinal conditions (~40% at pH 6.8 with pancreatin). In CaCo-2 cells treated with H_2O_2, Htyr-loaded nanoparticles enhanced cell viability up to 80% (at 20 µM), outperforming free Htyr (73%), likely due to synergistic radical-scavenging interactions between the bioactive compound and the zein matrix. Bioactivity preservation was further supported by the ORAC assay. Overall, this study highlights the potential of zein nanoparticles as a versatile formulation able of improving the stability and functional performance of Htyr. The combination of natural materials, robustness under processing conditions and preservation of bioactivity supports their application in next-generation pharmaceuticals, nutraceuticals and fortified foods enriched with phenolic antioxidants.



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Sciforum-210663: Advanced Formulation and Delivery Strategies for Next-Generation Dengue Vaccines: A Systematic Review

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Background: Dengue virus (DENV) infection remains a major global health concern, with four antigenically distinct serotypes requiring balanced and durable immune protection. Despite advances in vaccine development, challenges including serotype imbalance, antibody-dependent enhancement (ADE), variable immunogenicity, limited immune durability, and formulation instability remain significant.**Objective:** This systematic review evaluated recent pharmaceutical strategies for improving dengue vaccine development, focusing on advanced antigen engineering, delivery platforms, and formulation optimization technologies.**Methods:** A PRISMA 2020-based systematic review was conducted. PubMed, Scopus, and Web of Science were searched using predefined terms related to dengue vaccines, antigen engineering and antigen design, virus-like particles (VLPs), nanoparticles, mRNA platforms, delivery systems, and formulation technologies. Eligible studies were screened and analyzed based on vaccine platforms, delivery approaches, immunogenicity, safety characteristics, and formulation stability.**Results:** Among 1530 identified records, 46 studies were included in the qualitative synthesis. Evidence synthesis revealed three major strategies: antigen engineering, advanced delivery systems, and formulation optimization. VLPs, nanoparticle-based platforms, lipid nanoparticle (LNP)-mRNA systems, microneedle technologies, and thermostable formulations demonstrated potential to improve antigen presentation, delivery efficiency, immune responses, and vaccine stability.**Conclusion:** Advanced pharmaceutical technologies provide promising opportunities to overcome current limitations in dengue vaccine development. Integration of innovative antigen design, efficient delivery systems, and optimized formulations may contribute to safer, more effective, and accessible dengue vaccines. Further clinical validation and scalable manufacturing studies are required.

Author contributions: Methodology, Shahed Ahmadi;



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Sciforum-210762: Gamma irradiation mediated synthesis of silver nanoparticles in mesoporous silica particles for combined antimicrobial action

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Antimicrobial resistance (AMR) is a major global health challenge, driven by the increasing prevalence of multidrug-resistant microorganisms and the limited development of new antibiotics. Conventional antimicrobial therapy is often compromised by poor bioavailability, systemic toxicity, and inadequate drug concentrations at the infection site, highlighting the need for innovative delivery systems.

Mesoporous silica materials are promising nanocarriers due to their high surface area, tunable pore size, chemical stability, biocompatibility, and ability to provide controlled drug loading and release. In addition, silver nanoparticles (Ag NPs) exhibit broad-spectrum antibacterial activity through multiple mechanisms, including membrane disruption, reactive oxygen species generation, enzyme interference, and DNA damage. Their incorporation into mesoporous silica matrices may enhance nanoparticle stability and dispersion while enabling the simultaneous delivery of multiple antimicrobial agents. Radiation-induced synthesis provides a clean approach for the *in situ* formation of Ag NPs without additional reducing agents or high temperatures.

In this study, SBA-16 mesoporous silica was employed as a multifunctional carrier for the simultaneous incorporation of gamma-radiation-synthesized Ag NPs and two broad-spectrum antibiotics, chloramphenicol and bacitracin. The resulting systems were characterized by X-ray diffraction, nitrogen adsorption–desorption isotherms, scanning electron microscopy, and energy-dispersive X-ray spectroscopy. Their antimicrobial activity was evaluated using minimum inhibitory concentration and time-kill assays, while cytotoxicity assays were performed to assess biocompatibility.

Ag NPs were successfully synthesized and incorporated into the SBA-16 matrix. The combined Ag NPs/chloramphenicol/bacitracin systems demonstrated pronounced antimicrobial activity, as confirmed by MIC and time-kill assays, while cytotoxicity results supported their potential biocompatibility. Overall, these multifunctional systems represent a promising platform for enhanced antimicrobial therapy and an alternative strategy to address the growing challenge of AMR.

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Author contributions: Conceptualization, Andreea Simona Baltac; Methodology, Andreea Simona Baltac, Florina Zorila and Raul - Augustin Mitran; Formal analysis, Andreea Simona Baltac, Irina Atkinson, Daniela Culita, Daniel Negut, Raluca Elena Ginghina and Claudia-Ioana Draghici; Investigation, Andreea Simona Baltac, Irina Atkinson, Daniela Culita, Daniel Negut, Raluca Elena Ginghina, Claudia-Ioana Draghici, Florina Zorila and Raul - Augustin Mitran; Resources, Andreea Simona Baltac and Raul - Augustin Mitran; Data curation, Andreea Simona Baltac and Raul - Augustin Mitran; Writing - original draft, Andreea Simona Baltac; Writing - review and editing, Raul - Augustin Mitran; Visualization, Andreea Simona Baltac; Supervision, Raul - Augustin Mitran;



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Sciforum-210835: Resveratrol-loaded sericin-elastin nanoblends as innovative cosmeceutical formulation

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Upcycling agri-food and industrial byproducts into high-value bio-nanomaterials represents a promising route for sustainable drug delivery. In this work, we describe the development and the physico-chemical characterization of a topical nanoformulation made up of sericin (4 mg/mL), a silk degumming byproduct, and elastin (2 mg/mL), a biopolymer derived from human connective tissue, enriched with resveratrol (RSV), a winemaking-derived polyphenol.

The nanoblends showed an average diameter of 140 nm, a narrow size distribution, a Zeta potential of -35 mV and high stability at pH 7 and 10 and temperatures between 32 °C and 37 °C. Lyophilization with 10% mannitol preserved particle size and polydispersity index, while the Zeta potential shifted to -24 mV. Encapsulation of RSV (0.4 mg/mL) achieved an entrapment efficiency of ~30% (drug content 0.12 mg/mL) without altering nanoparticle size. The release studies showed biphasic kinetics reaching a maximum cumulative leakage of 90% after 24 h. The Higuchi model provided the best fit (), establishing Fickian diffusion as the primary release mechanism.

DPPH assay showed a superior radical scavenging activity for RSV-loaded nanoparticles compared to the free RSV (~63% vs ~36% at 10 µg/mL). In vitro tests on HaCaT cells confirmed the high biocompatibility of the formulation. RSV-loaded nanoblends demonstrated superior cytoprotection compared to the free drug (80–90% vs. 78–85% of cell viability at a drug concentration of 0.5-5 µM, respectively) when H_2O_2 was employed as an oxidant (700 µM). CellROX and MitoSOX assays confirmed the ability of RSV-loaded nanoblends to effectively reduce both intracellular and mitochondrial ROS production.

Finally, CompuSyn modeling validated strong carrier-drug synergy (CI $<$ 1), showing maximum efficiency at a drug concentration of 10 µg/mL with a Dose Reduction Index of 3.00. These results demonstrate the antioxidant potential of sericin-elastin nanoblends containing RSV as an innovative cosmeceutical system.



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Sciforum-210842: Resveratrol Niosomal Gel: Formulation Optimization, *In Vitro* Evaluation, and *Ex Vivo* Assessment

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Aim / Background

The present study focuses on the formulation and evaluation of a novel resveratrol (RSV) niosomal gel aimed at enhancing solubility, permeability, and sustained drug release.

Material and method

RSV-entrapped niosomes were formulated using the thin film hydration method and incorporated into a gel using carbopol-940 as the gelling agent. To optimize the formulation, a 3^2 factorial design was employed, varying the ratios of labrasol and cholesterol to achieve ideal niosomal characteristics. The RSV niosomes were assessed for particle size, entrapment efficiency, and in vitro dissolution profiles.

Result

Dynamic light scattering analysis revealed particle sizes ranging from 128 to 288 nm, zeta potentials of -27 to -15 mV, and drug release of 65-78%. The optimized formulation demonstrated an improved drug release of 78.17%, a small particle size of 128 nm, and a stable zeta potential of -14 mV, making it suitable for further development. The optimized niosomal formulation was then integrated into a gel, which was evaluated for both in vitro and ex vivo drug release. The in vitro release study using a dialysis membrane indicated enhanced diffusion and sustained release properties, with an 80% drug release after 24 hours. Ex vivo permeation studies revealed 71.4% drug release, demonstrating the potential for improved skin permeability and bioavailability.

Conclusion

These findings suggest that the use of a lipid mixture (labrasol and cholesterol) in the niosomal formulation not only enhances solubility and permeability but also provides a promising sustained-release system for resveratrol, making it a viable candidate for the treatment of inflammatory diseases. The advancements in formulation, coupled with comprehensive evaluation techniques, underscore the novelty of this study in addressing the challenges of resveratrol delivery through niosomal gels.

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Author contributions: Conceptualization, Shradha Shivdayal Tiwari; Methodology, Shradha Shivdayal Tiwari; Investigation, Shradha Shivdayal Tiwari; Resources, Shradha Shivdayal Tiwari; Data curation, Shradha Shivdayal Tiwari; Writing - original draft, Shradha Shivdayal Tiwari; Visualization, Shradha Shivdayal Tiwari; Project administration, Shradha Shivdayal Tiwari;



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Sciforum-210864: HSPiP Guided and QbD Optimization of Core-Shell Polymeric Nanoparticles for Enhancing the Delivery of Nutraceutical Bioactive Compound

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Silymarin is an antioxidant compound with multiple proven pharmacological benefits, but it faces several obstacles that hinder its full efficacy, including poor solubility and bioavailability, as well as a short half-life. Therefore, encapsulating SM in core-shell polymeric nanocapsules can overcome those obstacles and control its release, thereby improving SM properties overall. The HSPIP computational screening approach is a sustainable and inexpensive alternative to the standard wet-lab screening method, which is exceedingly costly, time-consuming, and associated with significant chemical and solvent usage. In this study, the HSPIP computational screening method was used to calculate the solubility of SM in 13 different liquid lipids. QbD (quality by design) was further used to optimize formulation parameters, resulting in the optimized formula SM-PLGA-PNCs. SM-PLGA-PNCs resulted in particle size of 58.09 ± 0.79, zeta potential of 16.4 ± 1.3, PDI of 0.246 ± 0.001, and EE% 98.3±0.006. It was characterized by TEM, which revealed a morphology of uniformly sized spherical capsules, with no visible agglomerates. Additionally, FTIR was conducted to evaluate drug interactions and chemical properties, and showed compatibility between SM and the polymer, confirming the successful encapsulation of SM in SM-PLGA-PNCs. An XRD study was also conducted, confirming the FTIR results. Moreover, an in-vitro release study comparing the SM suspension and SM-PLGA-PNCs demonstrated the controlled-release effect of the optimized formula relative to the SM suspension.

Author contributions: Conceptualization, Nahla Ahmed Elhesaisy, Shady Swidan, Mahmoud Teaima and Mohamed El-Nabarawi; Methodology, Nahla Ahmed Elhesaisy; Software, Nahla Ahmed Elhesaisy; Validation, Shady Swidan, Mahmoud Teaima and Mohamed El-Nabarawi; Formal analysis, Nahla Ahmed Elhesaisy; Investigation, Nahla Ahmed Elhesaisy; Data curation, Nahla Ahmed Elhesaisy; Writing - original draft, Nahla Ahmed Elhesaisy; Writing - review and editing, Shady Swidan, Mahmoud Teaima and Mohamed El-Nabarawi; Visualization, Shady Swidan, Mahmoud Teaima and Mohamed El-Nabarawi; Supervision, Shady Swidan, Mahmoud Teaima and Mohamed El-Nabarawi;



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Sciforum-210880: Development and characterization of an innovative two-component film-spray system for topical administration of hydroquinone.

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Hydroquinone (HQ) remains the gold-standard topical agent for skin hyperpigmentation disorders, but its clinical use is limited by pronounced physicochemical instability, particularly its high susceptibility to oxidative degradation. To overcome this limitation, an innovative two-component delivery system was developed, combining a polyvinyl alcohol (PVA)/glycerin polymeric film with an HQ solution applied as a spray, designed to minimize the exposure of HQ to oxidative effects. Three film formulations with varying PVA concentrations (1.5- 3%) were screened based on thickness, mass uniformity, and mechanical resistance. The 2.0% PVA formulation was selected and further optimized by reducing the glycerin content to 0.7%, yielding a uniform, mechanically stable film with adequate thickness (0.1800.022 mm), water absorption (108.875.09%), and surface pH (6.510.23) for topical use. The optimized HQ spray (2% HQ, 0.2% sodium metabisulfite, and purified water) delivered a consistent dose of 1.85 mg HQ/cm^2 per standardized application (five actuations over 4 cm^2). Over a 28-day stability study, refrigeration (4°C) of HQ solution markedly limited HQ oxidation compared with storage at 25°C (2.2% vs. 7.6% degradation), a trend paralleled by the pH profiles. Upon combination, spray application onto the film produced a slight, favorable decrease in surface pH (6.180.16), and ATR-FTIR analysis confirmed successful HQ incorporation into the polymeric matrix without major chemical alterations, consistent with predominantly physical incorporation and/or hydrogen-bonding interactions. These results support the two-component film-spray system as a promising strategy to overcome the oxidative instability of conventional HQ formulations, offering a novel approach for the topical delivery of oxidation-prone actives.

Author contributions: Validation, Carla Lopes and Maria Helena Amaral; Formal analysis, Rita Loureiro Carneiro; Investigation, Rita Loureiro Carneiro; Resources, Marlene Lúcio and Maria Helena Amaral; Data curation, Rita Loureiro Carneiro; Writing - original draft, Rita Loureiro Carneiro; Writing - review and editing, Carla Lopes, Marlene Lúcio and Maria Helena Amaral; Visualization, Carla Lopes and Maria Helena Amaral; Supervision, Carla Lopes and Maria Helena Amaral; Project administration, Maria Helena Amaral;



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Sciforum-210924: Chia Meets Chitosan: Nanomedicine for Lung Cancer

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Delivering anticancer agents directly to the lung offers an attractive opportunity to increase local drug exposure while reducing the limitations associated with systemic administration. Yet many promising bioactive compounds, including quercetin, remain difficult to translate because of poor aqueous solubility and limited bioavailability. Here, we developed an inhalable natural-polymer nanocarrier combining chitosan and *Salvia hispanica* (chia seed) polysaccharide to enhance quercetin delivery to lung cancer cells. Quercetin-loaded chitosan–chia polysaccharide nanoparticles were prepared as a natural polyelectrolyte complex and evaluated for physicochemical properties, drug incorporation, release, aerosol performance and anticancer activity. The optimized formulation contained quercetin at 0.01% w/v, chitosan at 0.04% w/v, and chia seed polysaccharide at 0.03% w/v. The resulting nanoparticles were quasi-spherical, with a mean hydrodynamic diameter of 331 ± 14.34 nm, low polydispersity (0.15) and a positive ζ-potential of +36.3 ± 2.56 mV. They achieved 73.8 ± 0.73% encapsulation efficiency and 14.20 ± 0.22% drug loading, while providing sustained biphasic quercetin release over 48 h. Importantly, aerosol testing produced a fine particle dose of 417.7 µg, supporting the pulmonary delivery potential of the formulation. Nanoencapsulation translated into enhanced biological activity. After 48 h, the IC_{50} of quercetin decreased from 197.4 to 78.8 µg/mL in A549 cells and from 69.7 to 56.5 µg/mL in H460 cells. Nanoparticle treatment also enhanced intracellular uptake and ROS-associated fluorescence and produced greater suppression of wound closure than free quercetin, while blank nanoparticles showed minimal cytotoxicity. Together, these findings demonstrate how chitosan and an underexplored plant-derived polysaccharide can be engineered into a functional inhalable nanoplatform, linking aerosol performance with enhanced intracellular delivery and anticancer activity. This proof-of-concept supports further investigation of chitosan–chia nanocarriers for localized lung cancer therapy.

Author contributions: Conceptualization, Sara Hasan and Emad L Izake; Methodology, Sara Hasan; Formal analysis, Sara Hasan; Investigation, Sara Hasan; Data curation, Sara Hasan; Writing - original draft, Sara Hasan; Writing - review and editing, Emad L Izake; Supervision, Emad L Izake; Project administration, Emad L Izake;



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Sciforum-210942: Olfactory deposition of Ibuprofen/Zolmitriptan-Loaded NLCs for Targeted Migraine Therapy

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Introduction: Migraine is a neurological disorder and current treatments often provide incomplete relief due to limited brain targeting. In this context, combining drugs and delivering them through the nose-to-brain route, which may facilitate access to the brain following deposition in the olfactory region, may improve therapeutic performance, particularly when supported by nanostructured lipid carriers (NLCs). This work aimed to develop a combined Ibuprofen/Zolmitriptan-loaded NLC formulation and evaluate its cytotoxicity and olfactory deposition *in vitro*.

Methods: The Ibuprofen/Zolmitriptan-loaded NLC was obtained by mixing the two previously optimised formulations (IBU-loaded and ZOL-loaded NLC), which were characterised for particle size (PS), polydispersity index (PDI), zeta potential (ZP) and encapsulation efficiency (EE). Cytotoxicity was assessed in differentiated neuronal SH-SY5Y cells. Olfactory deposition was evaluated in the 3D-printed nasal cast Aeronose® using four Aptar Pharma nasal spray devices (Neurospray™, Neurospray™ Preservative-Free, Cerespray™ Next-Gen and VP7/100+232).

Results: The Ibuprofen/Zolmitriptan-loaded NLC showed a PS of 98.980 ± 0.249 nm, a PDI of 0.242 ± 0.002 and a ZP of -15.143 ± 0.844 mV, with an EE of 84.376 ± 1.594 % for ibuprofen and 74.231 ± 0.646 % for zolmitriptan, demonstrating characteristics suitable for nose-to-brain delivery. The formulation showed no significant cytotoxicity up to 100 µg/mL in SH-SY5Y cells. Deposition studies revealed that the Neurospray™ achieved the highest deposition of the NLC formulation in the olfactory region (67.62 %), followed by the Neurospray™ Preservative-Free (64.34 %), Cerespray™ Next-Gen (52.63 %) and VP7/100+232 (14.80 %).

Conclusion: The Ibuprofen/Zolmitriptan-loaded NLC exhibited suitable characteristics and high olfactory deposition when administered using the Neurospray™ device, supporting its potential for nose-to-brain delivery in acute migraine therapy.



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Sciforum-210946: Development of Biocompatible Albumin Nanoparticles Using Sustainable Formulation Strategies

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Serum albumins have attracted interest as biomaterials for the targeted delivery of compounds.[1,2] As endogenous proteins, albumins are biodegradable, exhibit low toxicity, and are available. Their structural flexibility can be exploited to develop stimuli-responsive delivery systems for controlled release at the target site.[3] Albumin-based nanoparticles are commonly prepared by desolvation followed by chemical cross-linking, but organic solvents and synthetic cross-linking agents may raise toxicity concerns. [4]

In this study, we optimized and characterized albumin-based nanoparticles (NPs) developed through sustainable preparation routes—conventional desolvation and metal-induced self-assembly—using ethanol as the desolvating agent and glucose as cross-linking (2:1 and 1:1 protein:glucose weight ratios).

Bovine serum albumin (BSA)—commonly used as a model for human serum albumin (HSA)—and HSA were investigated to assess their influence on nanoparticle properties. Effects of albumin source and preparation method on size, polydispersity, surface charge, protein conformation and encapsulation efficiency were evaluated. Desolvation yielded BSA NPs of 140 ± 10 nm at a 2:1 ratio and 120 ± 7 nm at 1:1, with 7% protein incorporation. Circular Dichroism confirmed retention of BSA's native α-helical structure. Metal-assisted self-assembly (Cu^{2+}) increased protein incorporation to 12% (2:1) and 14% (1:1), while CD revealed increased negative ellipticity at 222 nm, reflecting Cu^{2+}-induced conformational rearrangements

Conversely, HSA yielded substantially larger nanoparticles via desolvation, 250 ± 20 nm (2:1) and 570 ± 20 nm (1:1). Cu^{2+} coordination resulted in uncontrolled aggregation and broad polydispersity, highlighting the limitations of considering BSA an interchangeable surrogate for HSA. Finally, quercetin encapsulation achieved 56% efficiency in desolvated BSA NPs and 65% in Cu^{2+}-assembled BSA NPs. These results validate glucose-stabilized albumin nanocarriers while highlighting structural constraints.

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Sciforum-210953: From bench to 500 mL: scale-up and characterization of nanostructured lipid carriers

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Nanostructured lipid carriers (NLCs) are effective vehicles for prolonged drug delivery, although scalable production methods are needed for commercial applications [1-3]. Increasing the formulation volume can affect particle size (PS) and polydispersity index (PDI), potentially compromising stability [2, 4].

In this work, NLC formulations were prepared in volumes ranging from 20 to 500 mL volumes and the process parameters were optimised to maintain a small PS and low PDI. NLCs were prepared using the ultrasound method described by Silva et al. [5]. Lipid and aqueous phases were heated and homogenised, and the resulting oil-in-water emulsion was sonicated and cooled to form the NLCs. The starting formulation was sonicated using a VCX 130 ultrasonic processor at 50% amplitude for 20 min, whereas the large-scale formulations were prepared using a Sonoplus® HD 4400, combining different amplitudes (20 and 50%) with different sonication times (5 to 20 min). PS and PDI were measured by dynamic light scattering (n=3, 25 °C).

At 20 mL, the PS was 82.5 ± 0.4 nm and the PDI was 0.226 ± 0.010. Among all combinations tested at the 500 mL scale, sonication at 20% amplitude for 15 min resulted in the smallest PS (107.8 ± 1.0 nm) and the lowest PDI (0.232 ± 0.008). Overall, appropriate adaptation of the process parameters and equipment enabled NLC production at the 500 mL scale while maintaining PS and PDI comparable to those of the small-scale formulation.

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Sciforum-210960: Biofunctional Polymer-Based Platforms for Controlled Delivery of STING Inhibitors

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The STING (stimulator of interferon genes) signaling pathway plays an important role in the regulation of innate immune responses and has emerged as a promising therapeutic target in conditions associated with excessive or dysregulated inflammation. The development of suitable delivery systems may improve the local availability of STING inhibitors and enable their controlled release. Therefore, the aim of this study is to develop and optimize polymer-based matrices as potential platforms for the delivery of STING-targeting compounds.

Several natural and synthetic polymer systems were screened with particular emphasis on their physicochemical stability and ability to maintain structural integrity during incubation. Among the investigated materials, albumin and poly(vinylpyrrolidone) (PVP) showed the highest potential. Albumin-based matrices containing 30% polymer were prepared using thermal crosslinking, while UV-induced crosslinking was also evaluated. PVP-based matrices containing 15% polymer were crosslinked by UV irradiation using polyethylene glycol diacrylate (PEGDA, Mn ≈ 700 g/mol) as a crosslinking agent and 2-hydroxy-2-methylpropiophenone as a photoinitiator. The developed materials were characterized in terms of their structural and surface properties, swelling behavior, degradation, and stability under incubation conditions.

Preliminary screening demonstrated clear differences in the stability of the investigated polymer systems. Several initially tested formulations rapidly lost their structural integrity or disintegrated during the early stages of incubation, whereas the selected albumin- and PVP-based systems maintained their geometry and remained stable during prolonged incubation. Moreover, incubation in simulated body fluids showed stable pH conditions over a 14-day period, indicating that the selected matrices did not induce substantial changes in the surrounding medium. Biofunctionalization in the present study refers to the incorporation of H-151, a STING inhibitor, directly into the polymer matrices during synthesis. H-151 was incorporated at a loading corresponding to a theoretical maximum concentration of 5 μM in the release medium, assuming complete release of the incorporated compound. H-151-containing formulations were successfully prepared, and studies evaluating its release from the selected matrices are currently in progress.

These preliminary results identify albumin- and PVP-based matrices as promising candidates for the further development of tunable polymer platforms for the delivery of STING inhibitors.

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Sciforum-210966: Application of Quality by Design (QbD) in Pharmaceutical Development of Fixed-Dose Combination Containing Herbal Extract and Synthetic Active Ingredient

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The development of fixed combinations (FCs) containing plant extracts and synthetic active pharmaceutical ingredients (APIs) is a promising area of modern pharmacy. However, the inherent variability of phytochemical composition creates challenges for quality assurance and regulatory compliance. The Quality by Design (QbD) paradigm provides a systematic framework for establishing a robust pharmaceutical development through the identification of critical quality attributes (CQAs), critical process parameters (CPPs), and the design space.

This study presents a QbD-oriented strategy for the pharmaceutical development of an FC containing a standardised extract of *Pelargonium sidoides* roots. The research approach includes comprehensive analytical characterisation of the extract using UHPLC-Q-TOF-MS/MS to identify key phytochemical markers. The marker profile serves as a basis for defining the CQAs of the plant-derived component. Additionally, the extract is subjected to *in vitro* biological activity screening to establish antimicrobial and antifungal activity for further justification of the selection of functional markers for efficacy control. Computer modelling is used to identify potential molecular targets of the identified markers, providing a rationale for the selection of pharmacodynamic markers.

The ultimate goal is to establish a multi-tier standardisation system: authenticity markers for raw material identification and functional markers for controlling pharmacological activity relevant to the target FC. This system enables the development of a robust analytical control strategy, supports stability studies, and facilitates the establishment of the design space for the FC composition. The proposed approach aligns with ICH Q8-Q11 guidelines and provides a science-based foundation for the QbD development of plant-synthetic FCs with predefined quality, safety, and efficacy profiles.

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Sciforum-210971: Polymers and Formulation Approaches for Floating In-Situ Gels

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Developing gastroretentive drug delivery systems using floating in-situ gels is an innovative strategy. These formulations are given as liquids and, once in the stomach, solidify into a gel that can stay buoyant for a long time. Polymers are important aspects of these systems as they affect gel formation, viscosity, gel strength, floating behaviour, and release of drugs. Due to their excellent gel-forming properties and biocompatibility, natural polymers such sodium alginate, pectin, guar gum, xanthan gum, and gellan gum are often studied. Additionally, viscosity, gel strength, and drug release characteristics can be altered by adding synthetic and semi-synthetic polymers. On the basis of the mechanism of gel formation, floating in-situ gels can be developed using different approaches, including ion-activated, pH-triggered, temperature-sensitive, and gas-generating systems. While suitable polymer combinations can enhance the quality and stability of the produced gel, gas-forming agents are especially helpful for adding buoyancy. The selection of polymer type, concentration, polymer combination, and gas-generating agent plays an important role in achieving suitable floating lag time, floating duration, and drug release. This work discusses the major polymers used in floating in-situ gels and the different formulation approaches employed to obtain effective gastroretentive systems.

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Sciforum-210974: Formulation Development and Evaluation of Kattha-Loaded Rectal Suppository for Hemorrhoidal Management

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Hemorrhoidal disease is a common anorectal disorder associated with local inflammation, irritation, and discomfort, highlighting the need for localized rectal delivery systems capable of providing prolonged residence and therapeutic activity at the site of application. *Acacia catechu* (Kattha) is a traditionally used medicinal plant rich in polyphenolic constituents and has been reported to possess antioxidant, anti-inflammatory, antimicrobial, and astringent properties. The present study aimed to develop and evaluate a Kattha-loaded polymeric suppository as a potential localized rectal drug delivery system for hemorrhoidal management. Kattha was incorporated into a natural polymer-based suppository matrix, followed by evaluation of its physicochemical, mechanical, structural, and biocompatibility characteristics. The developed suppositories were assessed for visual appearance, organoleptic properties, physical dimensions, weight variation, pH, content uniformity, breaking strength, swelling behavior, erosion, and rheological properties. Advanced characterization techniques, including Fourier-transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), thermogravimetric analysis (TGA), field-emission scanning electron microscopy (FESEM), scanning electron microscopy (SEM), atomic force microscopy (AFM), energy-dispersive X-ray spectroscopy (EDX), dynamic light scattering (DLS), and zeta-potential analysis, were employed to investigate the structural, morphological, thermal, elemental, and surface characteristics of the formulation. The optimized formulation demonstrated pH-responsive swelling, with swelling indices of 16.35%, 29.81%, 41.35%, and 51.92% at pH 4.5, 6.8, 7.4, and 8.0, respectively. The formulation exhibited gradual erosion, with its mass decreasing from 520 mg initially to 415 mg after 8 h, corresponding to approximately 20.2% erosion. Cytotoxicity evaluation using Caco-2 cells demonstrated 93–96% cell viability across 62.5–1000 μg/mL, with no significant morphological alterations. Overall, the findings indicate favorable physicochemical characteristics, hydration behavior, matrix integrity, and preliminary cytocompatibility of the Kattha-loaded suppository, supporting its potential as a localized rectal delivery platform. Further in-vitro drug-release, release-kinetic, mucoadhesion, ex-vivo permeation, stability, and in-vivo studies are required to establish its controlled-release performance and therapeutic efficacy.

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Sciforum-211000: Development and characterization of hydrogels containing fisetin-loaded nanostructured lipid carriers for melanoma treatment

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Melanoma is an aggressive form of skin cancer for which improved therapeutic strategies are still needed. Fisetin, a naturally occurring polyphenol with potential anticancer activity, has attracted increasing interest in melanoma research. However, its physicochemical properties may hinder effective delivery, making nanotechnology-based drug delivery systems, namely nanostructured lipid carriers (NLC), a promising approach. Because the liquid nature of NLC dispersions may limit their retention at the application site, incorporation into a semisolid formulation is recommended. Therefore, this work aimed to develop and characterize a hydrogel containing fisetin-loaded NLC (NLC-Fis) for topical application in melanoma. Unloaded NLC and NLC-Fis were prepared by emulsification of the molten lipid phase with an aqueous surfactant solution, followed by ultrasonication. Nearly spherical NLC and NLC-Fis exhibited mean particle sizes of 179.3 ± 2.8 and 214.8 ± 8.2 nm, respectively, with low polydispersity and suitable zeta potential, and remained physically stable for 90 days. Approximately 88% of the drug was incorporated, likely in an amorphous or molecularly dispersed state within the semicrystalline lipid matrix. This resulted in sustained release over 24 hours, unlike free fisetin, which was completely released within 4 hours. Both NLC dispersions were then gelled with Carbopol® 940 and characterized for color, texture, and rheological properties over 33 days. The hydrogels showed color stability even under light exposure and maintained favorable characteristics for application to the skin, including shear-thinning behavior that may facilitate spreading and good structural recovery. These findings highlight the potential of this formulation for topical fisetin delivery in melanoma.



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Sciforum-211011: Levofloxacin–pimelic acid multicomponent crystal: enhanced stability and biological properties

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Levofloxacin (LFX) is a third-generation synthetic fluoroquinolone antibiotic and the *L*-enantiomer of ofloxacin. In addition to its widespread clinical use as an antibacterial agent, LFX is considered a promising antitumor candidate. However, its practical utility is limited by chemical and physical instability: upon exposure to ambient moisture, LFX readily converts into an unstable hemihydrate, while light exposure in both the solid state and solution leads to degradation into inactive components, resulting in the loss of antibacterial activity. Photodegradation and hemihydrate formation can be effectively prevented through a multicomponent crystal strategy: molecular self-assembly, driven by complementary hydrogen-bond donors and acceptors, reconfigures intermolecular interactions to form a new crystalline phase, thereby modulating solubility, permeability, bioavailability, and stability. In this work, a novel solid form of LFX—a cocrystal with pimelic acid—was developed. The molecular and crystal structures were determined by single-crystal X-ray diffraction (SCXRD), and the material was further characterized using differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA). The cocrystal exhibited enhanced photostability and hydration resistance compared to pristine LFX. Antibacterial activity, evaluated via the serial dilution method against Gram-positive *Bacillus subtilis* and Gram-negative *Escherichia coli*, yielded a minimum inhibitory concentration (MIC) of 0.125 μg/mL for both microorganisms. These findings highlight the promise of this cocrystal as a stabilized pharmaceutical form of levofloxacin that maintains full antibacterial efficacy.



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Sciforum-211134: Polycation-stabilized alginate-based hydrogels for the regeneration of skin and mucous membranes

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Due to their favorable physicochemical and rheological properties, sodium alginate (SA)-based hydrogels are widely used as matrices for wound-healing dressings. Modification of alginate hydrogels with polycations, particularly PAMAM dendrimers, enables the formation of stable polyelectrolyte complexes and creates platforms for the immobilization and controlled release of bioactive compounds. Incorporation of porphyrins acting as superoxide dismutase (SOD) mimetics may reduce reactive oxygen species and oxidative stress and limit fibrous tissue formation. Therefore, this study aimed to evaluate polycation-stabilized SA hydrogels containing a porphyrin SOD mimetic as bioactive systems for wound healing and tissue regeneration.

The study utilized high-molecular-weight SA, third- and fourth-generation PAMAM dendrimers (G3 and G4), and Mn(III)TnHex-2-PYP (TPyp). Potentiometric titration showed a high degree of protonation of PAMAM primary amino groups at pH 7.4, reaching 98% for G3 and 85.53% for G4, confirming their cationic activity and ability to complex with SA. Formation of SA-PAMAM polyelectrolyte complexes was confirmed by FTIR spectroscopy and UV spectrophotometry. The possibility of incorporating TPyp into G3 and G4 dendrimers was subsequently investigated. Porphyrin release kinetics and the effects of the nature and concentration of calcium chloride and calcium sulfate crosslinkers on release from SA-PAMAM hydrogels were evaluated; the maximum released fraction reached 96.8%.

The biological properties of the developed hydrogel systems were then assessed. The hydrogels showed no significant cytotoxicity toward HaCaT keratinocytes and BJ-5ta fibroblasts. Under induced oxidative stress, treatment with hydrogel extracts reduced the proportion of DCFDA-positive cells from 56.31% to 11.41% in HaCaT cells and from 54.55% to 1.85% in BJ-5ta cells. In addition, the TPyp-containing system promoted macrophage polarization toward the anti-inflammatory M2 phenotype, indicating a potential pro-regenerative effect.

These results confirm the feasibility of developing a biocompatible porphyrin-containing system based on polycation-stabilized sodium alginate for accelerated regeneration of skin and mucous membranes.



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Sciforum-211190: A Practical Computational–Experimental Strategy for Drug–Polymer Phase Diagram Prediction and Validation

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We present an integrated computational–experimental workflow for the efficient construction of binary drug–polymer phase diagrams. COSMO-RS (Conductor-like Screening Model for Real Solvents) predicts solid–liquid equilibrium (SLE) curves, enabling screening and prioritization of candidate drug–polymer pairs for subsequent experimental validation. Prediction accuracy depends strongly on the quality of the input parameters, particularly the fusion thermodynamics of the drug, including melting temperature (T_m), enthalpy of fusion (ΔH_{fus}), and, where known, the change in heat capacity on fusion ($\Delta C_{p,\,fus}$). Accurate COSMO-RS calculations also require a representative molecular geometry, which is improved by identifying the relevant polymorph via powder X-ray diffraction and differential scanning calorimetry (DSC); experimental crystal structures (e.g., from the Cambridge Structural Database) provide a robust starting point for conformer generation. Experimental verification is performed using the DSC-based step-wise dissolution (S-WD) method, whereby a single supersaturated physical mixture is first used to determine the equilibration time at the lowest annealing temperature. The sample is then held at progressively higher temperatures, with the glass-transition temperature (T_g) measured after each step. Drug solubilities are obtained by mapping the measured T_g values onto a modeled composition–T_g relationship. Compared with the conventional melting point depression (MPD) approach, S-WD avoids the need for multiple sample compositions and mitigates ambiguities associated with onset/peak/offset T_m selection, as well as uncertainties in solubility equilibrium attainment. Together, COSMO-RS and S-WD streamline phase diagram construction, reduce experimental workload, and support the rational design of amorphous solid dispersions.

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Sciforum-211202: Integrated Computational and Experimental Investigation of LDPE Nanoplastic-Induced Destabilization of Polysorbate 80 Micellar Systems for Paclitaxel Delivery

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The increasing prevalence of nanoplastics has raised concerns about their potential interactions with nanoscale drug delivery systems and their effects on carrier stability and drug retention. This study combined MARTINI based coarse grained molecular dynamics with physicochemical characterization to investigate the influence of low density polyethylene nanoplastics on polysorbate 80 micelles used for paclitaxel delivery. Molecular dynamics systems containing 60 polysorbate 80 molecules and 9 paclitaxel molecules were simulated for 60 ns and compared in the presence and absence of LDPE nanoplastics. Structural organization and drug carrier interactions were evaluated using the principal moments of inertia, radius of gyration, solvent accessible surface area, root mean square deviation, radial distribution function, and energy analyses. In the absence of LDPE, the paclitaxel loaded micellar system remained relatively stable and showed moderate structural anisotropy, with a PMI anisotropy ratio of 0.236. The radius of gyration increased from approximately 2.8 nm for the polysorbate 80 micelle to 5.27 nm after incorporation of paclitaxel, while solvent accessible surface area values became relatively stable after about 40 ns. Radial distribution analysis showed a preferential association of paclitaxel with the hydrophobic tail region of polysorbate 80, with the strongest enrichment between 2.5 and 3.5 nm. RMSD and energy analyses further supported structural equilibration and reduced contact between paclitaxel and water. The presence of LDPE altered micellar organization and stability and showed behavior consistent with aggregation. Experimental characterization supported these observations. Synthesized LDPE nanoplastics smaller than 200 nm shifted the dominant DLS population from approximately 33.7 to 718.1 nm and changed the zeta potential from -11.3 to -32.3 mV. Overall, the findings indicate that LDPE nanoplastics can substantially alter the structural and colloidal behavior of polysorbate 80 micelles, with potential consequences for paclitaxel retention and release.

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Sciforum-211240: Smart Dual-Coated Polymersomes for Colon-Targeted Delivery of Repurposed Vardenafil in Ulcerative Colitis

Marwa Hamdy Sayed Dawoud [1,*], Nabila Mohamed Sweed [2], Islam Mohamed Salaheldin Mannaa [1], Salma Essam Ali Hassan [1], Nawal Medhat Abdelrahman [1], Verina Sameh Edward [1], Miriam Magdy Kamal Sedhom [1], Motaz Mohamed Abdelah Mohamed Ali Abouelkher [1], Farida Waheed Afifi Mohamed Hilal [1], Jessica Cherif Demian [1], Mariam maged youssef [1], Farida Ahmed Salaheldin [1] and Mariam Mohamed Fathy [1]

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Background: Ulcerative colitis (UC) is a chronic inflammatory bowel disease characterized by recurrent colonic inflammation and substantial morbidity. Effective management requires drug delivery that targets the colon while limiting premature release in the upper gastrointestinal tract. Vardenafil, a phosphodiesterase-5 inhibitor with reported anti-inflammatory activity, is a promising repurposed candidate for UC; however, its poor aqueous solubility and limited bioavailability may restrict therapeutic usefulness. Nanocarrier-based systems can improve drug incorporation, protect the drug during gastrointestinal transit, and enhance colonic localization.

Aim: This study aimed to develop, optimize, and dual-coat vardenafil-loaded PLGA polymersomes with chitosan and Eudragit S100 to provide sequential mucoadhesive, pH-responsive, and microbiota-responsive delivery to the colon.

Methods: Vardenafil-loaded PLGA polymersomes were prepared by emulsion solvent evaporation. A response surface design optimized the polymersomes in terms of the particle size and the entrapment efficiency. The optimized polymersomes were further coated with chitosan and Eudragit S100, then characterized for particle size, polydispersity index, zeta potential, and entrapment efficiency. The optimized dual-coated formulation was evaluated for *in-vitro* release, mucoadhesion, and pharmacokinetic performance.

Results: The optimized system formed dual-coated nanoparticles with a particle size of 206.17 ± 12.6 nm, PDI of 0.29 ± 0.01, zeta potential of +49.65 ± 9.54 mV, and entrapment efficiency of 70.43% ± 7.41. Drug release was limited in simulated gastric and intestinal fluids, with 19.8% ± 1.8 released within 5 h, followed by sustained release reaching 97.7% ± 2.8 after 24 h in simulated colonic fluid. Mucin interaction increased particle size 5.32-fold, indicating mucoadhesion. Compared with standard vardenafil, the nanoparticle formulation increased relative bioavailability 3.52-fold and prolonged residence time 7.19-fold.

Conclusion: Chitosan/Eudragit S100 dual-coated PLGA polymersomes provide a promising platform for colon-targeted vardenafil delivery. Their sequential coating combines mucoadhesive, pH-responsive, and microbiota-responsive properties, improving controlled release, and residence time, and supporting further investigation for UC therapy.

Author contributions: Conceptualization, Marwa Hamdy Sayed Dawoud and Nabila Mohamed Sweed; Methodology, Marwa Hamdy Sayed Dawoud, Nabila Mohamed Sweed, Islam Mohamed Salaheldin Mannaa , Salma Essam Ali Hassan , Nawal Medhat Abdelrahman, Verina Sameh Edward, Miriam Magdy Kamal Sedhom, Motaz Mohamed Abdelah Mohamed Ali Abouelkher , Farida Waheed Afifi Mohamed Hilal , Jessica Cherif Demian, Mariam maged youssef, Farida Ahmed Salaheldin and Mariam Mohamed Fathy; Software, Marwa Hamdy Sayed Dawoud, Nabila Mohamed Sweed and Islam Mohamed Salaheldin Mannaa ; Validation, Marwa Hamdy Sayed Dawoud, Nabila Mohamed Sweed, Islam Mohamed Salaheldin Mannaa and Salma Essam Ali Hassan ; Formal analysis, Marwa Hamdy Sayed Dawoud, Nabila Mohamed Sweed, Islam Mohamed Salaheldin Mannaa , Salma Essam Ali Hassan , Nawal Medhat Abdelrahman, Verina Sameh Edward, Miriam Magdy Kamal Sedhom, Motaz Mohamed Abdelah Mohamed Ali Abouelkher , Farida Waheed Afifi Mohamed Hilal , Jessica Cherif Demian, Mariam maged youssef,

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Sciforum-211319: Paeonol Nanoemulgel as a Novel Topical Approach for Accelerated Healing of Diabetic Wounds in Rats

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Diabetic wounds are characterized by persistent inflammation, oxidative stress, impaired angiogenesis, and delayed tissue regeneration. This study developed and evaluated a paeonol-loaded nanoemulgel for improving diabetic wound healing. The nanoemulsion was prepared using cinnamon oil, Cremophor RH 40, and Transcutol P and incorporated into a Carbopol 940 gel. The optimized formulation was characterized for particle size, polydispersity index, zeta potential, drug content, entrapment efficiency, pH, viscosity, in vitro drug release, ex vivo skin permeation, and stability. Its therapeutic efficacy was investigated in a streptozotocin–nicotinamide-induced diabetic excisional wound model in male Wistar rats. Animals were assigned to negative-control, vehicle-control, silver-sulfadiazine, paeonol-loaded nanoemulgel, and plain-paeonol groups. The optimized nanoemulgel exhibited satisfactory physicochemical stability, sustained drug release, enhanced skin permeation, and no clinically significant dermal irritation. Treatment with the paeonol-loaded nanoemulgel produced significantly greater wound contraction and a shorter epithelialization period than the negative-control, vehicle-control, and plain-paeonol treatments ($p < 0.05$). Histopathological examination demonstrated reduced inflammatory-cell infiltration, enhanced re-epithelialization, increased granulation-tissue formation, improved angiogenesis, and greater collagen deposition. Biochemical analysis revealed significant reductions in oxidative stress and the pro-inflammatory cytokines TNF-α and IL-1β, together with increased vascular endothelial growth factor expression ($p < 0.05$). These findings indicate that nanoemulgel-based topical delivery enhances the wound-healing activity of paeonol and represents a promising strategy for managing diabetic wounds.

Author contributions: Conceptualization, Shery Jacob and Shakta Mani Satyam; Methodology, Shery Jacob, Ibrahim Mustafa, Sai H. S. Boddu and Shakta Mani Satyam; Software, Ibrahim Mustafa and Sai H. S. Boddu; Validation, Ibrahim Mustafa, Sai H. S. Boddu and Shakta Mani Satyam; Formal analysis, Shery Jacob, Ibrahim Mustafa, Sai H. S. Boddu and Shakta Mani Satyam; Investigation, Ibrahim Mustafa and Shakta Mani Satyam; Resources, Shery Jacob, Sai H. S. Boddu and Shakta Mani Satyam; Data curation, Shery Jacob, Sai H. S. Boddu and Shakta Mani Satyam; Writing - original draft, Shery Jacob and Ibrahim Mustafa; Writing - review and editing, Shery Jacob, Ibrahim Mustafa, Sai H. S. Boddu and Shakta Mani Satyam; Visualization, Shakta Mani Satyam; Supervision, Shery Jacob, Sai H. S. Boddu and Shakta Mani Satyam; Funding acquisition, Shery Jacob;



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Sciforum-211326: Combinatorial Delivery of Cancer-Related siRNAs for Suppression of Breast Cancer Cell Proliferation by Electrostatically Stabilized Nucleopeptide Complexes

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Breast cancer is one of the most common oncological diseases among women. Although chemotherapy is a mainstay of its treatment, it reduces or eliminates fertility in women, necessitating alternative approaches. RNA interference has emerged as a promising strategy allowing suppression of oncogene expression. However, the key problem is siRNA delivery into target cells. Peptide carriers show considerable potential, providing efficient and specific siRNA delivery.

This work aimed to evaluate the efficacy of inhibiting breast cancer cell proliferation and migration via peptide-mediated combinatorial siRNA delivery.

The carrier system R6Hp/E9H4/E6p, composed of arginine, histidine, and glutamic acid residues, was formulated with siRNA at P/N/C (phosphate/nitrogen/carboxyl) ratios of 1/16/16 against COL4A2 and CDC20 targets responsible for proliferative activity in MDA-MB-231 triple-negative breast cancer cells. An inhibition of proliferation and migration was assessed using the resazurin test and the scratch assay.

Assessing the anti-proliferative activity of nucleopeptide complexes, a significant decrease in the number of viable cells was revealed compared to the control (complexes with non-targeted siRNA). The efficiency of proliferation suppression depended on the seeding density: the number of viable cells was reduced by 31% and 26% for cells seeded at low and high density, respectively ($p < 0.0001$). Cell migration assessment revealed that combinatorial transfection with nucleopeptide complexes reduced the number of migrated cells by 28% compared to the control ($p < 0.05$).

Thus, combinatorial delivery of siRNAs targeting CDC20 and COL4A2 via the R6Hp/E9H4/E6p carrier effectively inhibits MDA-MB-231 cell proliferation and migration, supporting further investigation of this system as a potential RNAi-based approach for breast cancer therapy.

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Sciforum-211408: Polymeric microneedles loaded with diacerein microsuspension for enhanced percutaneous drug delivery

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Background: Dissolving microneedles (DMNs) have emerged as a promising platform for percutaneous drug delivery due to their minimally invasive nature and self-administration. However, loading poorly water-soluble drugs into hydrophilic polymer matrices remains a major formulation challenge, often resulting in inadequate drug loading and suboptimal delivery. This study aimed to enhance the saturation solubility of Diacerein through microsuspension technology to improve its loading within polymeric DMNs.

Methodology: A Diacerein microsuspension (DM) was prepared via wet milling method in the presence of Tween 80 as a stabilizer and subsequently lyophilized. DM was incorporated into hydroxypropyl methylcellulose (HPMC) and polyvinylpyrrolidone (PVP) microneedle matrices (DM@MN) using a solvent-casting method. Characterization included particle size analysis, saturation solubility, scanning electron microscopy (SEM), mechanical performance, and Parafilm® M insertion testing. Accelerated stability studies were also conducted.

Results: DM showed a significantly reduced mean particle size (3.28 µm) and improved saturation solubility compared with the untreated drug. DM@MN demonstrated higher drug loading and better retention in the microneedle tips than untreated drug, supporting more efficient delivery potential. SEM imaging confirmed sharp, uniform needle structures. The microneedles effectively pierced excised animal skin and showed rapid polymer dissolution. The arrays showed better permeation (74.39%) and skin deposition (15.75%) after 24 hours, however, ~12% of the drug remained in the baseplate.

Conclusion: The microsuspension-based approach significantly enhances loading of Diacerein into dissolving polymeric microneedles. This strategy offers a practical pathway for improving the percutaneous delivery of other therapeutic agents with limited aqueous solubility.

Author contributions: Conceptualization, Maryam Shabbir; Methodology, Maryam Shabbir; Validation, Maryam Shabbir; Formal analysis, Uzair Nagra; Investigation, Uzair Nagra; Resources, Uzair Nagra; Data curation, Uzair Nagra;



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Sciforum-211444: Development of a Reconstitutable Fulvestrant Microparticle Injection with Release Comparable to the Castor Oil Formulation

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Fulvestrant is a selective estrogen receptor degrader used for hormone receptor-positive advanced breast cancer and is marketed as a high-viscosity castor oil-based intramuscular injection containing benzyl alcohol. This study aimed to develop an oil-free, reconstitutable fulvestrant microparticle formulation with sustained drug release comparable to the castor oil formulation. Microparticles were prepared by spray drying, with preliminary poloxamer 188/sodium carboxymethyl cellulose batches followed by optimization using zein, sodium alginate, and mannitol. Final batches F1–F4 contained 25% w/w fulvestrant, 40–60% w/w zein, 5–10% w/w sodium alginate, and 5–30% w/w mannitol, respectively, using ethanol:water (70:30) as the solvent system. F2–F4 produced fine, non-sticky powders with yields of 41.54–46.56%, drug contents of 95.52–98.34%, and reconstitution times of 40–63 s after reconstitution with Water for Injection. Scanning electron microscopy showed spherical microparticles with smooth surfaces and no visible agglomeration, while Fourier-transform infrared spectroscopy indicated no major drug–excipient incompatibility. Reconstituted suspensions showed pH values of 7.15–7.34 and satisfactory syringeability. Quantitative osmolarity was not measured; therefore, isotonicity was assessed microscopically using erythrocyte morphology against 0.9% sodium chloride control, with no swelling, shrinkage, or rupture observed. Sterility was evaluated by direct inoculation using Fluid Thioglycollate Medium and Soybean Casein Digest Medium, with no visible microbial growth after 14 days. No separate validated terminal sterilization process was applied to the spray-dried microparticles. F3, containing 50% w/w zein, was selected based on its balanced formulation performance and sustained release. F3 released 15.1% drug on day 1 and 97.4% by day 15, with a release profile comparable to the castor oil reference (f1 = 5.42; f2 = 69.74). After one month at 40 ± 2 °C/75 ± 5% RH, F3 retained 96.32% drug content and showed a reconstitution time of 73 ± 3 s. The developed microparticles represent a promising oil-free platform for reconstitutable fulvestrant depot injection; however, validated sterile manufacturing, quantitative osmolarity assessment, and in vivo pharmacokinetic and local tolerability studies are required for further development.

Author contributions: Conceptualization, Pranav Jogani and Dignesh Khunt; Methodology, Dhruti Sojitra; Formal analysis, Dhruti Sojitra; Investigation, Dhruti Sojitra and Pranav Jogani; Data curation, Pranav Jogani; Writing - original draft, Dignesh Khunt; Writing - review and editing, Dignesh Khunt; Visualization, Pranav Jogani; Supervision, Dignesh Khunt;



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Sciforum-211466: Cryo- and Lyoprotective Performance of Cholinium Amino Acid Ionic Liquids in TransfersomILs

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Lipid-based nanovesicles lose colloidal integrity during freezing and drying, which limits their shelf-life as delivery platforms. Ionic liquids (ILs) modulate interfacial interactions in nanocarriers, yet their cryo- and lyoprotective roles remain poorly described. This work established non-cytotoxic concentrations of two cholinium amino acid ILs and compared their protective performance in TransfersomILs against sugar-based protectants.

(2-Hydroxyethyl)trimethylammonium L-phenylalaninate [Cho][Phe] and (2-hydroxyethyl)trimethylammonium glycinate [Cho][Gly] were synthesised, and their cytotoxicity was evaluated in HaCaT keratinocytes by MTT assay after 24 h exposure (0.1–1%, v/v). For both ILs, 0.2% (v/v) was the highest concentration maintaining viability above the predefined 85% threshold. ILs were then incorporated into unloaded and caffeic acid-loaded TransfersomILs, caffeic acid being selected as a model bioactive for its antioxidant activity and limited stability. Size, polydispersity index, zeta potential, association efficiency and DPPH radical scavenging were measured before and after freezing at -5 °C for 4 h followed by thawing, and after freeze-drying (24 h, 0.6 mbar, same freezing step). Sucrose and mannitol, conventional protectants, were used as comparators at 0.2% (w/v), n=3.

ILs reduced vesicle size from 115 to 71–75 nm and raised association efficiency from 68% to 79–88%. After freeze–thawing, final/initial size ratios were 1.1–1.2 for IL-containing systems and 2.5 for the protectant-free control, matching the sugars, while caffeic acid retention reached 93–97%, exceeding both. After freeze-drying, IL size ratios increased to 1.6–1.8, above sucrose and mannitol (1.0–1.1), and retention fell to 89–94%.

Cholinium amino acid ILs act as effective cryoprotectants, outperforming sugars in caffeic acid retention upon freeze–thawing, but remain incomplete lyoprotectants. Elucidating the basis of this asymmetry, through thermal characterisation of the frozen systems and concentration–response protection studies, is the necessary next step.

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Sciforum-211502: Formulation and evaluation of self-micro emulsifying drug delivery system of atorvastatin calcium

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The present study focuses on the formulation and evaluation of a SelfMicroemulsifying Drug Delivery System (SMEDDS) of Atorvastatin Calcium to enhance its solubility and dissolution profile. Atorvastatin, a poorly watersoluble drug, was formulated using sunflower oil as the oil phase, Tween 80 as surfactant, and PEG 400 as co-surfactant. The prepared formulation wasevaluated for organoleptic properties, melting point, UV spectroscopy, solubility studies, pseudo-ternary phase diagram, FTIR, DSC, microscopic characteristics, globule size, zeta potential, and in-vitro dissolution study. The optimized SMEDDS showed good clarity and physical stability without phase separation for 35 days. FTIR and DSC studies confirmed compatibility between drug and excipients and indicated successful conversion of the drug into an amorphous form. The formulation exhibited a mean globule size of 173 nm with PDI 0.155 and zeta potential of –28.5 mV, indicating uniformity and stability. In-vitro dissolution studies demonstrated significantly enhanced drug release from SMEDDS (98.43% in 50 min) compared to pure Atorvastatin API (40.50%).The results concluded that the developed SMEDDS successfully improved the solubility, stability, and dissolution behaviour of Atorvastatin Calcium, thereby enhancing its potential oral bioavailability.



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Sciforum-211508: Phytochemical-Potentiated Chitosan Nanoparticles Against Multidrug-Resistant *Pseudomonas aeruginosa*

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Background and Objective: Multidrug-resistant (MDR) *Pseudomonas aeruginosa* remains a major cause of hospital-acquired infections, largely due to MexEF-OprN efflux-mediated resistance that reduces intracellular antibiotic accumulation. Curcumin and quercetin are natural efflux pump inhibitors (EPIs), but their clinical application is limited by poor solubility and bioavailability. The bojective ofg this study was to develop, optimize, and evaluate chitosan nanoparticles co-incorporating an antibiotic with curcumin or quercetin for efflux inhibition in MDR *P. aeruginosa*.

Materials and Methods: Nanoparticles were prepared by ionic gelation using chitosan and sodium tripolyphosphate (STPP). A 3^2 factorial design optimized chitosan (0.1–0.3%) and STPP (0.025–0.075%) concentrations with particle size and entrapment efficiency as critical quality attributes. Formulations were characterized for particle size, polydispersity index (PDI), zeta potential, entrapment efficiency, FTIR, DSC, FESEM, in vitro release, stability, and ethidium bromide (EtBr) accumulation.

Results: Optimized curcumin-loaded nanoparticles (0.2% chitosan, 0.05% STPP) exhibited a particle size of 205.7 nm, PDI of 0.39, zeta potential of +21.09 mV, and entrapment efficiencies of 82.2% and 75.8% for the antibiotic and curcumin, respectively. Quercetin-loaded nanoparticles showed a particle size of 283.0 nm, PDI of 0.74, zeta potential of +40.63 mV, and entrapment efficiencies of 83.4% and 79.1%, respectively. Although the formulations displayed relatively broad particle size distributions, a characteristic feature of ionic gelation-based chitosan systems, they maintained positive surface charge, colloidal stability, spherical morphology, sustained drug release for up to 16 h, enhanced EtBr accumulation, and physicochemical stability over three months.

Conclusion: Phytochemical-potentiated chitosan nanoparticles enhanced efflux inhibition and intracellular retention, demonstrating potential as a nanotherapeutic strategy for overcoming efflux-mediated resistance in MDR *P. aeruginosa*.

Author contributions: Conceptualization, Eknath D. Ahire and Pritam Kande; Methodology, Eknath D. Ahire and Pritam Kande; Software, Eknath D. Ahire and Pritam Kande; Validation, Pritam Kande; Formal analysis, Eknath D. Ahire; Data curation, Eknath D. Ahire; Writing - original draft, Eknath D. Ahire; Supervision, Eknath D. Ahire;



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Sciforum-211536: Photocrosslinkable Hyaluronic Acid-Based Hydrogels for In Situ Drug Delivery and Biomedical Applications

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Localized drug delivery and minimally invasive treatment require biomaterials that can be formed in situ while providing spatial control over material localization and therapeutic drug release. Here, we developed a photocrosslinkable platform based on glycidyl methacrylate-modified hyaluronic acid (GMA-HA) for in situ hydrogel formation under mild conditions.

Two photoinitiation strategies were investigated to enable selectable, tissue-depth-adapted activation. UV-mediated crosslinking at 365 nm using lithium phenyl-2,4,6-trimethylbenzoylphosphinate (LAP) enabled rapid gelation of GMA-HA formulations. To expand the platform toward less superficial applications, a red-light-activated system operating at 660 nm was developed using a phosphorus phthalocyanine/β-mercaptoethanol initiating pair. Incorporation of the cationic porphyrin $[(TPP)P(OEt)]^{+}Br^{-}$ was required to achieve high gel-volume conversion and additionally enabled fluorescence-based tracking of hydrogel localization through the skin using 450 nm excitation.

The LAP-based UV-crosslinked formulation was further evaluated in vivo: application to critical-size calvarial defects in Balb/c mice demonstrated substantial defect coverage (quantified by micro-CT) and low local inflammation, assessed by histology, supporting its suitability for in situ biomedical applications.

Overall, the developed GMA-HA photocrosslinking systems provide selectable photoactivation (UV and red light) and in situ hydrogel formation with potential for localized therapeutic delivery, sustained release, and optical monitoring. The combination of hyaluronic acid-based biomaterials with visible-light activation may provide a versatile platform for minimally invasive drug delivery and potential theranostic applications.

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Author contributions: Conceptualization, Sochilina Anastasia Vladimirovna and Evgeniya Alexandrovna Safonova; Methodology, Maksim Yurievich Suchkov, Sochilina Anastasia Vladimirovna, Egor Gorshkov and Evgeniya Alexandrovna Safonova; Validation, Maksim Yurievich Suchkov and Roman Akasov; Formal analysis, Maksim Yurievich Suchkov, Sochilina Anastasia Vladimirovna and Evgeniya Alexandrovna Safonova; Investigation, Maksim Yurievich Suchkov; Resources, Maksim Yurievich Suchkov, Egor Gorshkov, Inessa Andreevna Efimova and Evgeniya Alexandrovna Safonova; Data curation, Maksim Yurievich Suchkov and Sochilina Anastasia Vladimirovna; Writing - original draft, Maksim Yurievich Suchkov; Writing - review and editing, Sochilina Anastasia Vladimirovna, Nikita Grigorievich Yabbarov and Roman Akasov; Visualization,

Maksim Yurievich Suchkov and Inessa Andreevna Efimova; Supervision, Nikita Grigorievich Yabbarov; Project administration, Nikita Grigorievich Yabbarov and Evgeniya Alexandrovna Safonova; Funding acquisition, Evgeniya Alexandrovna Safonova;



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Sciforum-211614: Narrowing the Experimental Space: Quality by Design-Guided Early-Stage Development of Lipid–Polymer Hybrid Nanoparticles

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Background: Lipid–polymer hybrid nanoparticles (LPHNPs) combine the structural advantages of polymeric nanoparticles with the biomimetic surface properties and biocompatibility of lipid carriers, making them promising vehicles for parenteral drug delivery. However, their physicochemical properties depend heavily on complex formulation and process variables, necessitating systematic development approaches.

Aims: This study aimed to establish an early-stage Quality by Design (QbD) workflow for LPHNPs prepared by nanoprecipitation, demonstrating how preliminary experimentation can support risk-based reduction of the experimental space.

Materials and Methods: A preliminary Quality Target Product Profile (QTPP) was defined for a parenteral LPHNP platform. Critical Quality Attributes (CQAs) were identified, and potential Critical Material Attributes (CMAs) and Critical Process Parameters (CPPs) were selected. Risk assessment was performed to prioritise variables for preliminary experimental screening. LPHNPs composed of poly(lactic-co-glycolic acid (PLGA) and phospholipids (phosphatidylcholine and 1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC)) were prepared via nanoprecipitation using organic solvents (acetonitrile or acetone for the polymer, and ethanol for the lipids). The effects of solvent and dialysis medium type, DPPC content, lipid-to-polymer ratio, and preparation temperature on particle size, polydispersity index, and zeta potential were evaluated.

Results: The dialysis medium did not significantly alter the key CQAs; thus, 10% phosphate-buffered saline was selected as a practical standard. Based on the CQA profiles, a preparation temperature of 60°C and a 1:5 lipid-to-polymer ratio were chosen to establish an optimal baseline. A pronounced solvent–lipid composition interaction was observed: increasing DPPC content was well-tolerated in acetonitrile-based formulations, whereas a 50% DPPC lipid ratio in acetone-containing formulations led to significant particle enlargement and high polydispersity.

Conclusions: Integrating risk assessment with preliminary experimentation efficiently supports QbD-based LPHNP development. This approach enables rational prioritisation of formulation and process variables, exclusion of unfavourable formulation regions, and definition of a focused experimental space for subsequent multivariate Design of Experiments optimisation.

Author contributions: Conceptualization, Zsófia Németh, Gábor Katona and Ildikó Csóka; Methodology, Zsófia Németh and Bence Sipos; Software, Zsófia Németh; Validation, Zsófia Németh and Bence Sipos; Formal analysis, Gábor Katona; Investigation, Zsófia Németh, Mohammadamin Ebrahimi and Fruzsina Kecső; Resources, Bence Sipos, Gábor Katona and Ildikó Csóka; Data curation, Zsófia Németh, Mohammadamin Ebrahimi and Fruzsina Kecső; Writing - original draft, Zsófia Németh, Mohammadamin Ebrahimi and Fruzsina Kecső; Writing - review and editing, Bence Sipos, Gábor Katona and Ildikó Csóka; Visualization, Zsófia Németh, Mohammadamin Ebrahimi and Fruzsina Kecső; Supervision, Zsófia Németh; Project administration, Zsófia Németh;



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Sciforum-211633: Development and characterization of hydrogel-based insulin delivery systems for topical use

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INTRODUCTION. Preclinical and clinical studies indicate that topical insulin may accelerate wound healing by promoting cell proliferation, collagen synthesis, re-epithelialisation, and angiogenesis while reducing inflammation and oxidative stress. The development of effective insulin-containing hydrogels remains challenging. This study aimed to develop and evaluate insulin-loaded hydrogels for potential application in skin regeneration and repair. Two carriers were investigated: sodium alginate and a sodium alginate–hyaluronic acid combination.

MATERIALS AND METHODS. Hydrogels containing 1 mg/g insulin (Insulatard® Penfill®) were prepared according to the 12th edition of the Polish Pharmacopoeia using sodium alginate (F1) or sodium alginate with hyaluronic acid (F2). In vitro insulin release was evaluated using a paddle apparatus with Enhancer Cell™ chambers and a Strat-M® membrane. Rheological properties were determined using an RM 200 Touch rotational rheometer (Lamy Rheology Instruments). We assessed the spreadability of insulin-containing hydrogels using the two-glass method at loads of 20–700 g by measuring the radius of a 300 mg sample after 30 seconds. The pH of the hydrogels was determined using the potentiometric method with a SevenCompact™ S210 pH meter. The hydrogels remained stable during 4 weeks' storage at 25±1°C and 5±3°C, in accordance with the ICH Q5C guidelines.

RESULTS. The formulations developed were characterised by a prolonged insulin release profile. The bioavailability of insulin from the hydrogels was 60.11% over 7 hours (F1) and 55.88% over 8 hours (F2). Rheological analysis showed that the resulting preparations are non-Newtonian, shear-thinning fluids with thixotropic properties. The best fit was obtained for the Herschel–Bulkley model (a pseudoplastic fluid with a yield point). Hydrogels based on sodium alginate and sodium alginate, and hyaluronic acid containing insulin are characterised by comparable spreadability and a pH value within the optimal range for the skin (pH = 7.18 and pH = 7.42, respectively).

CONCLUSIONS. The pre-formulation studies carried out indicate that the hydrogel matrices developed represent a promising system for the local delivery of insulin; however, they require further investigation, including an assessment of their cytotoxicity and biocompatibility.

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Sciforum-211813: Formulation and Optimization of Cetirizine Orodispersible Films Using Experimental Design Approaches

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Introduction: Orodispersible films (ODFs) represent an innovative and patient-friendly dosage form designed to disintegrate rapidly within the oral cavity without requiring water administration. This technology significantly enhances patient compliance, particularly among pediatric and geriatric populations. This study aimed to formulate, evaluate, and optimize an ODF loaded with 10 mg of Cetirizine Dihydrochloride (CTZ-ODF) to achieve rapid disintegration and suitable mechanical robustness.

Methods: ODFs were manufactured via the solvent casting method. An initial preformulation screening evaluated five hydrophilic film-forming polymers (PVA, HPMC K4M, HPMC E5, HPMC E15, and Gelatin) alongside three superdisintegrants (Crospovidone, Sodium Starch Glycolate [SSG], and Croscarmellose Sodium). Sorbitol was investigated as a plasticizer at concentrations ranging from 0% to 20%. Two in vitro disintegration testing methodologies (*Petri dish method* vs. *Frame-and-Ball method*) were critically compared. Subsequently, an I-Optimal Mixture Design (Design-Expert® 13) was implemented to optimize the key components: HPMC E15 (X1), Glycerol (X2), and SSG (X3).

Results: Screening identified HPMC E15 as the optimal polymer, conferring balanced transparency, flexibility, and rapid disintegration capability. The *Frame-and-Ball* technique demonstrated superior reproducibility and mechanical discrimination compared to the Petri dish method. Statistical optimization yielded a target optimal formulation comprising 45.61% HPMC E15, 11.12% Glycerol, and 3.16% SSG. The optimized CTZ-ODF exhibited an ultrafast disintegration time of 27 seconds, alongside optimal mechanical integrity and physical stability.

Conclusion: Integrating preformulation screening with an I-Optimal design successfully produced a robust, rapidly disintegrating cetirizine oral film. This platform shows strong promise for industrial scale-up in oral fast-dissolving delivery systems.

Author contributions: Conceptualization, Radjaa Nafissa DJELIEL; Software, Djawad CHIKH; Validation, Djawad CHIKH; Formal analysis, Radjaa Nafissa DJELIEL; Investigation, Radjaa Nafissa DJELIEL; Resources, Djawad CHIKH; Writing - review and editing, Djawad CHIKH; Supervision, Djawad CHIKH;



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Sciforum-211966: Green-by-Design Biodegradable Elastomeric Implants for Solvent-Free, Long-Acting Protein Delivery

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Introduction: Sustainable pharmaceutical manufacturing requires delivery technologies that reduce hazardous solvents, energy-intensive processing, and persistent material waste without compromising therapeutic performance. This study evaluates biodegradable poly(diol-co-tricarballylate) (PDT) elastomers as a green-by-design platform for localized, long-acting protein delivery.

Methods: PDT elastomers were synthesized by mild polycondensation of tricarballylic acid and aliphatic diols, followed by acrylation and visible-light photocrosslinking. Interleukin-2 (IL-2) was incorporated in solid form without organic solvents. Release behavior, protein bioactivity, polymer degradation, and antitumor efficacy were evaluated, with release modulation achieved through crosslinking density, excipient composition, and implant geometry.

Results: The PDT matrices provided tunable, near-linear sustained IL-2 release through an osmotic-driven mechanism. IL-2 retained $>$90% bioactivity during the first month of release. Controlled elastomer degradation generated minimal acidic by-products, supporting biocompatibility while avoiding ultraviolet irradiation and solvent-based protein processing. In vivo, sustained subcutaneous IL-2 delivery prevented tumor growth in a murine Renca carcinoma model.

Conclusions: Visible-light-cured PDT elastomers integrate solvent-free protein loading, biodegradable materials, mild fabrication conditions, and long-acting therapeutic delivery within a single platform. These findings support PDT implants as a sustainable approach to advanced biologic formulation and controlled release.

Author contributions: Conceptualization, Husam M Younes; Methodology, Husam M Younes; Software, Husam M Younes; Validation, Husam M Younes; Formal analysis, Husam M Younes; Investigation, Husam M Younes; Resources, Husam M Younes; Data curation, Husam M Younes; Writing - original draft, Husam M Younes; Writing - review and editing, Husam M Younes; Visualization, Husam M Younes; Supervision, Husam M Younes; Project administration, Husam M Younes; Funding acquisition, Husam M Younes;



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Sciforum-212690: Synthesis, Biological Evaluation, and Molecular Modeling Studies of Novel Chalcone–Pyridinium–Hydrazone Hybrids

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Molecular hybridization, which integrates two or more pharmacophores within a single molecular framework, has emerged as a useful strategy for developing compounds with improved biological and drug-like properties. In this study, a novel series of 10 chalcone–pyridinium–hydrazone hybrids (2a–j), incorporating a cinnamamide-derived unit, a quaternized pyridinium moiety, and a hydrazone linkage, was designed and synthesized via a two-step synthetic route. The structures of the synthesized compounds were confirmed by ^{1}H-NMR and ^{13}C-NMR spectroscopy. Cytotoxicity was evaluated in HUVEC and BEAS cells using MTT and SRB assays, while antioxidant-related effects were assessed using DPPH, glutathione (GSH), and total antioxidant status (TAS) assays. The compounds showed limited cytotoxicity in the tested normal cell models, while significant changes were observed in selected antioxidant-related parameters, including total protein content and TAS. To further assess their pharmacological potential, in silico evaluation using SwissADME, pkCSM, and ProTox-3.0 identified the 2-pyridyl and 2-furyl derivatives as the most favorable candidates in terms of predicted drug-like properties, with a bioavailability score of 0.55. However, predicted interactions with P-glycoprotein and potential hERG II inhibition were identified as liabilities across the series. SwissTargetPrediction suggested cholinesterases as potential molecular targets, while molecular docking indicated plausible interactions with acetylcholinesterase and butyrylcholinesterase. Overall, these findings identify chalcone–pyridinium–hydrazone hybrids as promising candidates for further investigation, particularly with respect to their antioxidant potential, pharmacological properties, and possible cholinesterase-related activity. Additional experimental studies are required to confirm their molecular targets and optimize their efficacy and safety profiles.

Author contributions: Conceptualization, Ebru Nur AY; Methodology, Ebru Nur AY; Software, Ebru Nur AY; Validation, Ebru Nur AY; Formal analysis, Ebru Nur AY; Investigation, Ebru Nur AY; Resources, Ebru Nur AY; Data curation, Ebru Nur AY; Writing - original draft, Ebru Nur AY; Writing - review and editing, Ebru Nur AY; Supervision, Ebru Nur AY; Project administration, Ebru Nur AY; Funding acquisition, Ebru Nur AY;



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Sciforum-214075: Polyphenol Extracts from *Glycyrrhiza glabra* L.: Encapsulation, Chemical Characterization, and Evaluation of Anti-Inflammatory, Anti-Proliferative, Oral, and Intraperitoneal Activities

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This study analyzes the therapeutic properties of polyphenolic extracts from *Glycyrrhiza glabra* L. (licorice) and the efficacy of their nanoencapsulation in liposomes produced via microfluidic technology, a strategy developed to overcome the poor stability and low aqueous solubility of free phytocompounds. Phytochemical analysis revealed a profile rich in specific flavonoids and chalcones, such as liquiritin and glabridin. In biological assays, the extract-loaded liposomes (GG-Lipo) exhibited marked selective cytotoxicity against three human colorectal cancer cell lines (HT29, SW480, and CaCo2), drastically reducing their viability without affecting healthy human colonic epithelial cells (HCECs). Furthermore, the liposomal system demonstrated excellent immunomodulatory and antioxidant properties both *in vitro* and *in vivo*, significantly reducing lipid peroxidation and the levels of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6), while restoring endogenous enzymatic defenses such as superoxide dismutase, catalase, and glutathione peroxidase. Regarding analgesic activity, animal models of chemical and thermal nociception confirmed the ability of the nanoencapsulated formulation to suppress both peripheral and central pain via supraspinal mechanisms, matching or exceeding the performance of reference drugs like acetaminophen. Finally, the 14-day toxicological evaluation highlighted that encapsulation flattens toxic plasma peaks, thereby preventing the systemic shock and mortality observed with high doses of the free extract administered intraperitoneally, validating the safety and biocompatibility of the lipid matrix for future clinical applications against cancer and related painful inflammatory conditions.



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Session 10. Biopharmaceutics, Disposition, Pharmacokinetics and Pharmacodynamics

Sciforum-205000: Physiologically Based Pharmacokinetic (PBPK) Modelling of a Gastroretentive Cimetidine Formulation: Predicting Enhanced Bioavailability Through Prolonged Gastric Retention.

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IntroductionCimetidine's clinical utility is limited by its short half-life (~2 h) and narrow absorption window. Gastroenteric drug delivery systems (GRDDS) can overcome these limitations, but development typically requires costly in vivo studies. This study used PBPK modelling (PK-Sim® v11.3) to predict how a pH-responsive buoyant in situ gelling system modulates cimetidine absorption.

MethodsSimulations incorporated cimetidine's properties (pKa 6.8, logP 0.78). As PK-Sim® provides no African population database, an African-American database served as a proxy, with selected parameters adjusted to reflect assumed gastrointestinal conditions (gastric pH 1.5–2.5, gastric emptying $>$ 2 h, intestinal transit, CYP450 metabolism, renal clearance); these are modelled assumptions, not established physiology. Gastric retention was modelled by modifying gastric emptying; pH-responsive release was represented by a formulation-specific release profile; and gel integrity was represented as a sustained retention assumption, as PK-Sim® does not mechanistically model viscosity. The GRDDS (sodium alginate 4% w/v, calcium carbonate 1% w/v, assumed viscosity ≥ 3000 cP, buoyancy $>$ 8 h) was simulated as a single arm.

ResultsThe model predicted a GRDDS AUC of 27,106 µmol·min/L, a Cmax of 14.31 µmol/L, a tmax of 1.4 h, an MRT of 32.08 h (vs 4–6 h for conventional tablets), and an apparent terminal half-life of 20.11 h (absorption-limited, not a change in intrinsic clearance). The model predicted a 92% probability of maintaining plasma concentrations above the established minimum therapeutic level of 0.5 µg/mL for $>$12 h, providing a modelling-based rationale for further evaluation of twice-daily dosing. Gastric emptying was the most influential variable; extending retention from 2 to 8 h increased AUC by 34%. Because the simulation modelled only the GRDDS formulation, no model-derived comparator was available; published data for gastroretentive cimetidine systems report approximately 2.3-fold increases in systemic exposure relative to conventional tablets (Mishra et al., 2025; Rovati et al., 1983), though direct comparison should be interpreted cautiously.

DiscussionThe simulated GRDDS showed favourable predicted exposure and prolonged MRT. Prospective experimental validation, including a model-derived conventional tablet comparator, is required.



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Sciforum-208367: Acebutolol Attenuates Glycoxidative Stress and Alters mTOR-Associated Phosphoprotein Signaling in Hyperglycemic HUVECs

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Hyperglycemia promotes endothelial glycoxidative stress and is accompanied by alterations in intracellular signaling. This study investigated whether acebutolol attenuates hyperglycemia-induced glycoxidative injury and alters the phosphorylation of proteins associated with PI3K/Akt/mTOR signaling in human umbilical vein endothelial cells (HUVECs). HUVECs were cultured for 7 days under hyperglycemic conditions induced by 30 mM D-glucose and treated with acebutolol at concentrations of 20–100 μg/mL. Glycation- and glycoxidation-related endpoints, protein oxidation, oxidative stress, caspase-3 activity, and phosphorylation of eight signaling proteins were assessed. Data were normalized to the hyperglycemic control and analyzed using one-way ANOVA followed by Dunnett's test. At 100 μg/mL, acebutolol significantly reduced markers of glycation, glycoxidation, protein oxidation, and oxidative stress by 23–41% ($p < 0.05$), including total advanced glycation end products (AGEs), argpyrimidine, pentosidine, N-formylkynurenine, advanced oxidation protein products, amyloid cross-β structures, and NADPH oxidase activity. Caspase-3 activity was not significantly increased. At 20–80 μg/mL, acebutolol significantly altered the phosphorylation of several proteins associated with PI3K/Akt/mTOR signaling. The most pronounced effects were observed for p-S6RP, p-mTOR, p-BAD, and p-IRS1, whose relative phosphorylation signals decreased to 0.7–21.4% of the hyperglycemic control, defined as 100%. Significant reductions were also observed for p-GSK3α/β, p-p70S6K, and p-PTEN, whereas p-Akt was not significantly affected. At 100 μg/mL, reductions in several phosphoproteins were less pronounced than at lower concentrations, indicating a non-monotonic response pattern. Overall, acebutolol attenuated hyperglycemia-associated glycoxidative injury and altered the phosphorylation profile of proteins associated with PI3K/Akt/mTOR signaling in endothelial cells.

Author contributions: Conceptualization, Szymon Drygała and Mateusz Maciejczyk; Methodology, Szymon Drygała, Kamila Karpienko and Mateusz Maciejczyk; Validation, Szymon Drygała and Mateusz Maciejczyk; Formal analysis, Kamila Karpienko and Mateusz Maciejczyk; Investigation, Szymon Drygała, Kamila Karpienko and Mateusz Maciejczyk; Resources, Mateusz Maciejczyk; Data curation, Szymon Drygała and Mateusz Maciejczyk; Writing - original draft, Szymon Drygała; Writing - review and editing, Szymon Drygała and Mateusz Maciejczyk; Visualization, Szymon Drygała and Kamila Karpienko; Supervision, Mateusz Maciejczyk; Funding acquisition, Mateusz Maciejczyk;



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Sciforum-210808: Can simple UV-Vis measurements with tryptophan serve as a screening model for potential drug-AGP interactions?

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Alpha-1-acid glycoprotein (AGP) is a key plasma protein involved in the binding and transport of numerous drugs, particularly basic compounds. The aim of this study was to evaluate whether simple UV-Vis measurements using tryptophan as a model component of the AGP binding site could serve as a screening method for assessing **potential drug-AGP binding interactions**. Thirty drugs with diverse chemical structures were analyzed. UV-Vis spectra were recorded for the drug alone, tryptophan alone, and the drug-tryptophan mixture and the experimental mixture spectra were compared with theoretical additive spectra. A series of parameters describing deviations from additivity, including U, RB, RW, L+W - L and L+W - Add were calculated and subjected to statistical analysis.

The parameters U, RB and RW **consistently identified the same group of 12 drugs** showing evidence of interaction with tryptophan. Paroxetine represented a **borderline interaction**, suggesting a weaker effect than that observed for the remaining compounds. Relationships were also observed between the spectrophotometric parameters and selected physicochemical descriptors, particularly polar surface area and the HOMO–LUMO energy gap. Multiple and logistic regression analyses indicated that selected physicochemical properties contributed to the differentiation between interacting and non-interacting compounds. Overall, the results suggest that UV-Vis measurements with tryptophan may provide a simple screening approach for the preliminary assessment of **potential drug-AGP binding interactions**, particularly when combined with physicochemical and chromatographic descriptors.

Author contributions: Conceptualization, Karolina Wanat; Methodology, Karolina Wanat; Software, Karolina Wanat; Validation, Elżbieta Brzezińska; Formal analysis, Karolina Wanat; Investigation, Agata Siniarska; Resources, Agata Siniarska; Data curation, Karolina Wanat; Writing - original draft, Karolina Wanat and Agata Siniarska; Writing - review and editing, Elżbieta Brzezińska; Visualization, Karolina Wanat; Supervision, Elżbieta Brzezińska; Project administration, Karolina Wanat; Funding acquisition, Elżbieta Brzezińska;



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Sciforum-210881: Pharmacokinetic Changes of Calcineurin Inhibitors During Pregnancy: Importance of Therapeutic Drug Monitoring

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Background: Pregnancy induces physiological changes that can alter the pharmacokinetics of calcineurin inhibitors (CNIs), potentially affecting whole-blood concentrations and dose requirements. Close therapeutic drug monitoring (TDM) is therefore essential to maintain appropriate immunosuppressive therapy during pregnancy and the early postpartum period. Objective: To characterize changes in CNI concentrations and dose requirements during pregnancy and the early postpartum period, and to highlight the role of TDM in guiding individualized dose adjustment.

Methods: We retrospectively analyzed clinical and TDM data from pregnant patients who had undergone renal transplantation or were treated for nephrotic syndrome with a CNI. The study included five pregnancies. Whole-blood trough concentrations (C0) of tacrolimus and cyclosporine were monitored throughout pregnancy and after delivery. CNI doses and concentrations were evaluated longitudinally, and dose adjustments were performed according to TDM results and the clinical context. Results: CNI trough concentrations progressively declined during pregnancy, despite dose adjustments, with reductions of approximately 50–95% compared with pre-pregnancy levels and the most pronounced decreases occurring during the second and third trimesters. Dose requirements increased progressively in some cases, with a maximum increase of approximately 88% (1.9-fold) from baseline. Following delivery, CNI concentrations increased markedly, reaching several-fold higher levels than those observed during late pregnancy, prompting subsequent dose adjustments. These findings highlight substantial fluctuations in CNI exposure and dose requirements throughout pregnancy and the early postpartum period.

Conclusion: Pregnancy induces substantial changes in CNI exposure and dose requirements. Close TDM throughout pregnancy and the early postpartum period is essential to guide individualized dose adjustments and maintain therapeutic CNI exposure.

Author contributions: Conceptualization, Mekaouche Fatima Zohra Nadjet; Methodology, Mekaouche Fatima Zohra Nadjet; Investigation, Mekaouche Fatima Zohra Nadjet; Writing - original draft, Mekaouche Fatima Zohra Nadjet; Writing - review and editing, Mekaouche Fatima Zohra Nadjet;



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Sciforum-210997: Cyclodextrin-Engineered Quercetin as a Translational Delivery Platform: A Critical Evidence Synthesis Linking Supramolecular Complexation with Pharmacokinetic and Pharmacodynamic Outcomes

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Quercetin (QCE) is a pharmacologically pleiotropic flavonol whose clinical development is challenged by poor aqueous solubility, chemical instability, extensive pre-systemic metabolism, and low, variable systemic exposure. This critical mechanistic review examines how cyclodextrin (CD) engineering improves biopharmaceutical performance and how these improvements relate to available pharmacokinetic (PK) and pharmacodynamic (PD) evidence. Published studies of β-CD, its hydroxypropyl, sulfobutylether, and methyl derivatives, and γ-CD were examined for complex stoichiometry, binding stability, solid-state properties, solubility, dissolution, permeability, and available exposure and response outcomes. Representative β-CD systems increased aqueous solubility approximately 2.2 to 4.6-fold, while selected hydroxypropyl-β-CD formulations achieved increases approaching 630-fold. Lyophilised hydroxypropyl-β-CD complexes investigated for nasal delivery increased solubility approximately 14 to 50-fold across pH 1.2 to 6.8 and enabled measurable ex vivo permeation across rabbit nasal mucosa, where uncomplexed QCE showed negligible transport. These study-specific findings reflect different formulations and experimental conditions, rather than a direct comparison of CD performance. In eight healthy participants, an isoquercitrin (QCE-3-O-glucoside)–γ-CD formulation showed approximately 10.5-fold higher relative bioavailability than quercetin formulated in dextrin. This result does not isolate the contribution of CD complexation from that of glycosylation or establish therapeutic efficacy. Mechanistic contributors include host–guest inclusion, reduced crystallinity, enhanced apparent aqueous solubility, and molecular stabilisation. Reversible complexation also influences the availability of unbound drug for membrane permeation. However, solubility enhancement alone does not ensure proportional exposure or therapeutic response. We therefore propose a CD–QCE Formulation–Exposure–Response framework linking supramolecular interactions and biopharmaceutical properties with PK disposition and PD outcomes. The framework supports formulation-specific CD selection and identifies the need for matched exposure–response studies, route-specific safety assessment, and clinical validation when developing QCE systems for neurodegenerative, infectious, and oncological applications.

Author contributions: Conceptualization, Mahendra Pratap Swain; Methodology, Mahendra Pratap Swain; Validation, Ashok Kumar Pattnaik; Formal analysis, Ashok Kumar Pattnaik and Sandeep Kumar Singh; Investigation, Mahendra Pratap Swain; Resources, Mahendra Pratap Swain; Data curation, Mahendra Pratap Swain; Writing - original draft, Mahendra Pratap Swain; Writing - review and editing, Mahendra Pratap Swain; Visualization, Ashok Kumar Pattnaik and Sandeep Kumar Singh; Supervision, Ashok Kumar Pattnaik and Sandeep Kumar Singh;



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Sciforum-211001: Dosing Inhibition: The Conformational Effect of 1 vs. 2 Dicumarols on NQO1-FAD Inhibition

Ingryd Carolly de Oliveira Medeiros [1,*], Antenor Correia da Silva Júnior [1], Carlos Augusto de Senna Azevedo [1], Ludmilla da Silva Augusto [1], Giovanna Isabelle Camilo [2], José Maria Sombra Júnior [1], Leticia Nogueira Gurgel de Oliveira [1], Dayane Aurora dos Santos Fernandes [1], Mayke Sombra Barbosa [1], Eveline Matias Bezerra [1] and Roner Ferreira da Costa [1]

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The overexpression of NAD(P)H oxidoreductase 1 (NQO1) in different tumor types has highlighted this enzyme as a potential therapeutic target. Among the known inhibitors of NQO1 is dicoumarol, a coumarin derivative that binds to the enzyme's active site, competes with the NAD(P)H cofactor, and inhibits its catalytic activity. Although the interaction of dicoumarol with NQO1–FAD is known, conformational changes associated with the number of ligands present in the complex remain poorly explored. Therefore, this study used molecular dynamics (MD) simulations to investigate NQO1–FAD systems containing one and two dicoumarol molecules, aiming to compare the stability and flexibility of the ligand. Molecular dynamics simulations were performed using the crystal structure of the NQO1–FAD–dicoumarol complex (PDB ID: 2F1O) as the starting structure, using GROMACS 2025.4, the AMBER99SB-ILDN force field, and the SPC/E water model. Systems containing one or two dicoumarol molecules were neutralized with Na^+ and Cl^- ions at a concentration of 0.15 mol/L and subjected to energy minimization until the maximum force was below 100.0 kJ/mol. Equilibration was initially performed under the NVT ensemble at 300 K, followed by the NPT ensemble using the Parrinello–Rahman barostat. The resulting trajectories were analyzed using root-mean-square deviation (RMSD), root-mean-square fluctuation (RMSF), radius of gyration (Rg), and principal component analysis (PCA), allowing the influence of the presence of one or two dicoumarol molecules on the conformational behavior of NQO1–FAD to be assessed. The results demonstrated differences in the stability and conformational flexibility of the systems containing one and two dicoumarol molecules. RMSD, RMSF, Rg, and PCA analyses indicated that the number of ligands influences the dynamics of the NQO1–FAD complex, suggesting different conformational patterns as a function of dicoumarol occupancy.



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Sciforum-211205: Chimeric form of GM-CSF in the treatment of burn wounds in rats

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Thermal burns are a leading cause of injury, resulting in up to 300,000 deaths annually (WHO). The primary causes of mortality following burns are secondary infection and shock, driven by the disruption of the epithelial barrier and increased vascular permeability. Cytokines and growth factors play an important role in wound healing, significantly reducing healing time. Granulocyte-macrophage colony-stimulating factor (GM-CSF) is being actively investigated as a therapeutic agent for treating wounds of various etiologies; however, its clinical application is limited by adverse reactions and in vivo instability. In this study, using a rat model of burn injury, we investigated the wound-healing properties of a recombinant form of GM-CSF fused with human apolipoprotein A-I (GM-CSF-ApoAI) to enhance stability. The wound-healing efficacy of the chimeric protein was assessed by measuring changes in wound area, histological analysis, and the expression of genes encoding cytokines, angiogenesis markers, and markers of the wound-healing process. The treatment by chimeric GM-CSF accelerated the transition from the inflammatory phase toward the proliferative/repair phase, characterized by resolution of neutrophilic infiltration and increased macrophage and fibroblast presence. Furthermore, GM-CSF-ApoAI treatment increased Angpt1/Angpt2 mRNA ratio, consistent with histological data, which may indicate earlier formation of mature blood vessels. The chimeric GM-CSF promoted earlier wound epithelialization, resulting in a 1.5-fold increase in epidermal thickness by day 25 of the experiment compared to controls. The reduction of inflammation and normalization of blood supply to the wound bed under the influence of GM-CSF-ApoAI may facilitate the remodeling of scar tissue within a shorter timeframe.

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Sciforum-211294: A biomimetic chromatographic and computational approach to the rate of drug passage through the Blood-Brain Barrier

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Compounds' affinity for the CNS is expressed using different parameters, including:

i) log ***BB*** (the ratio of the total, equilibrium drug concentration in the brain to that in blood)

ii) log ***PS*** expressed in [mL/min/g brain] and obtained *via in situ* brain perfusion studies using the Renkin-Crone equation: $PS = -F \ln(1 - K_{in}/F)$, where F is the cerebral blood or perfusion flow rate, $K_{in} = (Q_{br}/Q_{pf})/T$ is the unidirectional transfer constant, Q_{br} is the concentration, corrected for the vascular volume, of compound in the brain, Q_{pf} is the concentration of a compound in the perfusion fluid, and T is the perfusion time

iii) the unbound brain-to-plasma concentration ratio ($K_{p,uu,brain}$) and the unbound CSF (cerebrospinal fluid)-to-plasma concentration ratio ($K_{p,uu,CSF}$).

In this study, log ***PS*** was predicted for a group of 21 drugs based on experimental reference data. It was established that log ***PS*** is related to the Immobilized Artificial Membrane (IAM) chromatographic retention parameter obtained with 100% aqueous mobile phases, log k_{IAM}^{w} – for the correlation between log ***PS*** and log k_{IAM}^{w}, Pearson's R = 0.74 (vs. R = 0.51 for the relationship between log ***PS*** and the Micellar Liquid Chromatographic retention data obtained using sodium dodecyl sulfate-based micellar mobile phases). It seemed therefore likely that log ***PS*** can be predicted using a combination of IAM chromatographic and calculated descriptors. A model of log ***PS*** proposed in this study involved log k_{IAM}^{w} and computational descriptors ***TPSA*** (Topological Polar Surface Area), ***Mw*** (Molecular Weight), and (***N+O***) (the total count of N and O atoms). The coefficients for ***TPSA*** and M_w are negative, suggesting that excessive polarity and molecular size reduce the rate of BBB passage.

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Sciforum-211420: Cannabidiol and Δ^9-Tetrahydrocannabinol in Polypharmacy: Mapping the Potential Clinically Significant Interactions

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Background: Cannabidiol (CBD) and Δ9-tetrahydrocannabinol (THC) are main phytocannabinoids in Cannabis sativa L. CBD is non-intoxicating, whereas THC produces psychoactive effects. Both undergo extensive hepatic metabolism, primarily involving CYP3A4, CYP2C9, and CYP2C19, and may also inhibit metabolic enzymes and drug transporters. Aim: To identify database-classified potential significant interactions of CBD and THC with medicines used in pharmacotherapy and characterize their principal clinical mechanisms. Methods: Potential drug interactions were identified using the drugs.com Interaction Checker in September, 2026. The database was searched using the terms "cannabidiol" and "cannabis (THC-containing products)" to assess their database-classified potential interactions with other medicinal products. The identified interactions were categorized according to severity as major, moderate, or minor. The analysis focused primarily on interactions classified as major. Results: Cannabidiol was associated with 26 major, 667 moderate, and 32 minor potential interactions, whereas THC-containing products were associated with 28 major and 379 moderate interactions. Selected major CBD-interacting medicines included buprenorphine, colchicine, citalopram, doxorubicin, edoxaban, ketoconazole, ketamine, lomitapide, methadone, morphine, mipomersen, pexidartinib, teriflunomide, and venetoclax. The underlying risks included altered drug exposure through CYP450 or P-glycoprotein modulation, additive hepatotoxicity, QT prolongation, bleeding, and central nervous system (CNS) depression. Major THC interactions occurred predominantly with opioids and CNS depressants, including alfentanil, brexanolone, codeine, fentanyl, hydromorphone, ketamine, oxycodone, remifentanil, tapentadol, and tramadol, potentially resulting in profound sedation and respiratory depression. Conclusion: Among the major interactions identified, CBD interactions appear primarily pharmacokinetic or toxicity-related, whereas THC interactions are predominantly pharmacodynamic. Concomitant use warrant avoidance when possible or careful clinical management, or managed through medication review, individualized dose adjustment, and appropriate clinical and laboratory monitoring. Prospective studies are required to distinguish predicted interactions from clinically confirmed risks.

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Sciforum-212684: Substrate-Dependent Reversal of Inhibition and Activation by Hyperbolic Enzyme Modifiers

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A compound's effect on enzyme activity is frequently assigned as fixed inhibition or activation, independent of the substrate concentration used to measure it. Within the general modifier (Botts–Morales) framework, this characterization becomes conditional whenever a modifier's two coefficients — α, governing substrate binding, and β, governing the catalytic step — act in opposing directions relative to unity. For such a modifier, $v/v_0 = (1 + \beta x/\alpha)(1 + \sigma)/(1 + \sigma + x + \sigma x/\alpha)$, with $\sigma = [S]/K_M$ and $x = [X]/K_x$. Setting $v/v_0 = 1$ yields a crossover substrate concentration $\sigma^* = (\alpha - \beta)/(\beta - 1)$, which is positive and physically accessible when the condition for sign reversal is met. A critical and underappreciated consequence follows directly from the form of σ^*: because it depends only on α and β, and not on modifier concentration, a complete modifier titration at a fixed substrate concentration produces a convincing dose–response curve while leaving the substrate-dependent inversion entirely undetected. Using published α and β values from three characterized enzyme–modifier systems, we show that σ^* falls within accessible substrate ranges, so the same compound is correctly described as a partial inhibitor at one substrate concentration and as an activator at another. This reversal, an exact consequence of the general modifier scheme, has received little attention in the enzyme-activation literature. We propose that a minimal substrate series should be included in the characterization of any modifier assigned a fixed mechanistic classification

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