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CONFERENCE ABSTRACTS

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Drug delivery and manufacturing

Compatibility and Stability-indicating tests for fixed-dose combination antituberculosis drugs

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Background: Tuberculosis (TB) remains a major global public health concern, and its treatment requires prolonged multidrug therapy, which is frequently associated with poor patient adherence, suboptimal treatment outcomes, and the emergence of drug-resistant strains. To simplify therapy and improve patient compliance, the World Health Organisation recommends fixed-dose combination (FDC) tablets that incorporate rifampicin, isoniazid, pyrazinamide, and ethambutol. Despite the therapeutic advantages, the chemical stability of these FDCs is a persistent challenge. Rifampicin, in particular, is known to undergo degradation in combination with other anti-TB drugs, leading to reduced potency, potential treatment failure, and increased risk of resistance development. Understanding the physicochemical behaviour of these active pharmaceutical ingredients (APIs), especially in relation to moisture interactions and solid-state compatibility, is crucial for improving formulation stability, ensuring consistent drug quality, and safeguarding patient health.

This study aimed to systematically investigate the moisture sorption characteristics and solid-state compatibility of rifampicin, isoniazid, pyrazinamide, and ethambutol within four-drug FDC formulations. The primary objective was to determine whether moisture uptake and drug–drug interactions could account for the reported instability of these combination tablets, thereby informing strategies to enhance formulation robustness.

Method: Gravimetric vapour sorption (GVS) analysis was employed to evaluate the moisture sorption properties of individual APIs under controlled relative humidity (RH) conditions ranging from 0% to 90% at 25°C. Isothermal microcalorimetry (IMC) was used to assess the compatibility of the four APIs, both individually and in combination, at 40°C, in the presence and absence of elevated humidity (75% RH). API combinations were prepared in ratios corresponding to a commercially available four-drug FDC formulation. Heat flow data from IMC experiments were analysed for signs of potential chemical or physical interactions indicative of incompatibility.

Results: GVS analysis showed that rifampicin, isoniazid, and pyrazinamide exhibited relatively stable moisture sorption behaviour across the tested RH range, although rifampicin underwent a phase transformation at higher humidity levels. Ethambutol displayed pronounced hygroscopicity and underwent deliquescence at RH ≥75%, confirming its high sensitivity to moisture. IMC analysis demonstrated no measurable incompatibilities among the four APIs at 40°C, regardless of humidity conditions. Observed heat flow profiles aligned closely with theoretical non-interaction predictions, suggesting the absence of detectable solid-state incompatibilities under the experimental conditions.

Conclusion: These findings highlight the highly hygroscopic nature of ethambutol but indicate that moisture sorption alone is unlikely to fully explain the instability of four-drug anti-TB FDCs. Microcalorimetric data suggest that rifampicin, isoniazid, pyrazinamide, and ethambutol are compatible in the solid state at 40°C, even under humid conditions. The results imply that other factors, such as polymorphic transformations, higher-temperature interactions, or manufacturing-related variables, may contribute to rifampicin degradation. Further investigations, including advanced solid-state characterisation techniques such as X-ray powder diffraction, are warranted to fully elucidate the mechanisms underlying instability in four-drug FDC formulations.

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Local delivery of steroids to inner ear via medical device INCAT (the Inner Ear Catheter) in partial deafness patients during cochlear implantation: Preliminary results

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Background: Intracochlear administration of steroids may be beneficial in preserving residual hearing in patients with partial deafness undergoing cochlear implantation (CI).

Method: The aims of the study were to evaluate the effectiveness and safety of steroid administration using the Inner Ear Catheter (INCAT) in partial deafness treatment (PDT) patients undergoing CI, and to assess the impact of INCAT insertion depth on hearing preservation (HP) after implantation. Inclusion criteria were adult patients qualified for CI with severe or profound hearing loss according to the PDT classification. Exclusion criteria included age under 18 years, comorbidities, and concomitant pharmacotherapy potentially interacting with steroids. The study was approved by the ethics committee. Ten patients (5 women and 5 men), aged 40–70 years (mean age 53.2 years), were enrolled. Three steroid administration protocols were applied: 1.Methylprednisolone 62.5 mg/ml (solution) – 3 patients, 2. Methylprednisolone 40 mg/ml (suspension) – 4 patients, 3. Dexamethasone 4 mg/ml (solution) – 3 patients. The study was conducted at the International Center of Hearing and Speech in Kajetany, Poland. Statistical analysis included the Shapiro–Wilk test for normality, the Wilcoxon test for paired samples to compare hearing thresholds before CI and at CI activation, the paired t-test to compare electrode impedance, and the χ^2 test to assess relationships between hearing preservation, steroid use, and INCAT insertion depth. Statistical significance was set at $p < 0.05$.

Results: At CI activation, complete hearing preservation (CHP) was observed in 2 patients (20%), partial HP in 5 patients (50%), and minimal HP in 3 patients (30%). The most favorable outcomes were achieved in the methylprednisolone 40 mg/ml group, where 50% of patients achieved CHP and 50% partial HP, with no cases of minimal HP. Less favorable outcomes were observed in the dexamethasone group, while the least favorable results occurred in the methylprednisolone 62.5 mg/ml group. Shallower INCAT insertion depth was associated with better hearing preservation.

Conclusion: Preliminary results suggest that methylprednisolone 40 mg/ml may provide superior hearing preservation outcomes in partial deafness patients undergoing cochlear implantation.

Spatially programmed bilayer microneedles enable dual-center hierarchical drug delivery for synergistic therapy of androgenetic alopecia

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Background: Androgenetic alopecia (AGA) is one of the most prevalent dermatological conditions globally, and its clinical treatment is predominantly hindered by two critical challenges: low drug bioavailability and the difficulty in achieving synergistic intervention in multiple key hair follicle cells. The follicular microenvironment possesses a naturally compartmentalized structure, where core functional cells such as hair follicle stem cells (HFSCs) and dermal papilla cells (DPCs) are spatially segregated and play distinct roles in regulating hair growth cycles. Conventional homogeneous microneedles (MNs), which deliver drugs in a non-targeted manner, lack the spatial targeting capacity required to adapt to this compartmentalized follicular microenvironment, thus limiting their therapeutic efficacy. Therefore, the development of a spatially targeted drug delivery system that can achieve on-demand and synergistic regulation of key follicular functional zones is urgently needed for effective AGA management. This study aims to develop a spatially programmed bilayer MN system to address the limitations of current AGA therapies. The core objective is to realize on-demand and synergistic intervention in key follicular functional zones via a dual-center hierarchical delivery strategy. Specifically, the system is designed to match the spatial distribution of HFSCs and DPCs, enabling targeted delivery of different therapeutic agents to their respective action sites, thereby enhancing local drug utilization, exerting synergistic therapeutic effects, and ultimately improving the overall efficacy of AGA treatment while reducing systemic side effects.

Method: The bilayer MN system was fabricated with a hierarchical structure: the upper layer was loaded with quercetin-ZIF-8 nanoparticles (targeting the HFSC compartment), while the lower layer's tips contained finasteride (FIN)-loaded lipid nanocarriers (targeting the DPC region). The spatial drug release profile and transdermal properties of the MNs were characterised. In vitro effects on HFSC activation and DPC function were evaluated, and in vivo therapeutic efficacy and toxicity were assessed in an AGA mouse model, with minoxidil and homogeneous drug delivery systems as controls.

Results: The fabricated bilayer MNs achieved on-demand hierarchical drug release, with quercetin-ZIF-8 nanoparticles targeting HFSCs to exert antioxidant and anti-inflammatory effects and activate stem cells, while FIN-loaded nanocarriers locally inhibited dihydrotestosterone (DHT) production in the DPC region. In vivo studies confirmed that the bilayer MN system outperformed minoxidil and homogeneous drug delivery systems, showing reduced systemic toxicity and significantly improved therapeutic outcomes, including enhanced hair regrowth.

Conclusion: The developed spatially programmed bilayer MN platform achieves spatially guided and on-demand drug delivery tailored to the functional partitioning of the follicular microenvironment. By realizing synergistic intervention in two key follicular cell compartments (HFSCs and DPCs) through a dual-center hierarchical delivery strategy, this system effectively enhances local drug utilization, exerts comprehensive therapeutic effects (including stem cell activation, antioxidant, anti-inflammatory, and DHT inhibition), improves therapeutic efficacy, and reduces systemic toxicity. These findings indicate that the spatially programmed bilayer MN system provides a novel and promising strategy for the effective management of AGA, with great potential for clinical translation.

Construction of a subcutaneous sustained-release system of rapamycin-loaded lemon-derived extracellular vesicles and its therapeutic study for AGA

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Background: Androgenetic alopecia (AGA) is the most common form of progressive hair loss, characterised by follicular miniaturisation and premature senescence of dermal papilla cells (DPCs), ultimately leading to hair follicle regression and thinning of the scalp. Currently approved pharmacological treatments, such as finasteride and minoxidil, offer limited therapeutic efficacy and are often associated with adverse effects or poor long-term patient compliance. Accumulating evidence suggests that excessive oxidative stress and impaired autophagy play key roles in DPC senescence and hair follicle degeneration during AGA progression. Consequently, the development of safe and effective therapeutic strategies specifically targeting these pathogenic mechanisms remains an important and unmet clinical need. Plant-derived extracellular vesicle-like nanoparticles have recently attracted considerable attention due to their excellent biocompatibility, intrinsic bioactivity, and potential as natural nanocarriers for dermatological therapy.

Method: A rapamycin-loaded lemon-derived extracellular vesicle system, rapamycin-loaded lemon-derived extracellular vesicles (LEVs-RAPA), was developed and systematically evaluated using in vitro and in vivo models. Lemon-derived extracellular vesicle-like nanoparticles were isolated and loaded with rapamycin via electroporation. Human DPCs were treated to assess cellular uptake and subsequent biological responses. Intracellular reactive oxygen species (ROS) levels, autophagy-related signalling pathways, and hair follicle-associated markers were analysed to determine antioxidant, anti-senescent, and follicle-activating effects. A scratch wound assay evaluated DPC migratory capacity as an indicator of hair follicle microenvironment restoration. For in vivo studies, LEVs-RAPA was administered subcutaneously to a mouse model of AGA. Hair regrowth, hair density, and the proportion of hair follicles in anagen phase were quantified. Follicular cell proliferation was assessed via Ki67 immunostaining, and systemic biosafety was further evaluated by histological analysis of major organs, including the heart, liver, spleen, lungs, and kidneys.

Results: Rapamycin was successfully encapsulated, forming a stable and efficient LEVs-RAPA delivery system. In vitro, LEVs-RAPA markedly suppressed dihydrotestosterone-induced overactivation of the mammalian target of rapamycin (mTOR) signalling pathway and reduced intracellular ROS accumulation in DPCs. β-Galactosidase staining confirmed a significant reduction in the proportion of senescent cells. Scratch wound assays demonstrated enhanced DPC migration, suggesting improvement in the hair follicle microenvironment. In vivo, subcutaneous administration of LEVs-RAPA substantially promoted hair regrowth in AGA mice, as evidenced by increased hair density and a higher proportion of follicles transitioning from telogen to anagen phase. Histological analysis of major organs, including heart, liver, spleen, lungs, and kidneys, revealed no pathological abnormalities, indicating a favourable in vivo biosafety profile for the delivery system.

Conclusion: The rapamycin-loaded lemon-derived extracellular vesicle system (LEVs-RAPA) exerts synergistic therapeutic effects through intrinsic antioxidant activity combined with inhibition of the PI3K/Akt/mTOR signalling pathway. This dual mechanism effectively alleviates oxidative damage and premature senescence of DPCs, thereby promoting hair follicle activation and hair regeneration. Given its excellent biocompatibility and demonstrated pro-hair growth efficacy, LEVs-RAPA represents a novel and highly promising therapeutic strategy for AGA and provides a solid foundation for the further development of plant-derived extracellular vesicle-based drug delivery systems in dermatology.

Stability issues and quality risks of L-ascorbic acid tablets in tropical climates: A mixed-methods study of the Nigerian pharmaceutical supply chain

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Background: L-Ascorbic acid (Vitamin C) is a widely used antioxidant with recognized instability challenges, particularly under tropical conditions. Its degradation compromises therapeutic efficacy, especially in regions with inadequate storage and distribution infrastructure, like Nigeria.

Objectives: To confirm reported trends in the stability and quality of L-ascorbic acid tablets in the Nigerian pharmaceutical supply chain through stakeholder engagement and laboratory evaluation.

Method: A mixed-methods study was conducted involving 214 pharmaceutical stakeholders. Concurrently, nine NAFDAC-registered brands of L-ascorbic acid tablets were subjected to physicochemical and microbial testing's. The USP method was used for the assay. Stability testing was conducted over 30 days under accelerated conditions (40 ± 2 °C, 75 ± 5% RH).

Results: Over 90% of stakeholders reported observing colour changes and degradation in 100 mg L-ascorbic acid tablets. Laboratory tests revealed that 44.4% of brands showed initial colour non- conformance, and one brand (11.11%) failed. Observed quality issues may be linked to inadequate packaging and poor storage conditions.

Conclusion: Significant stability issues persist with L-ascorbic acid tablets in Nigeria. Regulatory enforcement, climate-adapted packaging, and robust supply chain controls are essential to enhance product integrity and safeguard public health.

3D-printed oral dissolving film platform enabling rapid-acting influenza nanovaccines for pandemic preparedness

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Background: Influenza viruses are transmissible respiratory pathogens with pandemic potential and global health concern. They are transmitted through the mucosal route. Although a couple of vaccines have been approved, most are administered intramuscularly, which is painful and can lead to vaccine hesitancy. In this proof-of-concept study, we investigated the immunogenicity of an adjuvanted microparticulate Influenza vaccine administered as oral dissolving film (ODF) via the mucosal route.

Method: Herein, we encapsulated the vaccine antigens, Inactivated Influenza A H1N1 virus (i-Influenza A H1N1) and Inactivated Influenza A H3N2 virus (i-Influenza A H3N2) in a biodegradable Poly (Lactic-co-glycolic acid) (PLGA) polymeric matrix. The adjuvant MF59(AddaVax™) was selected to enhance the immunogenicity of the antigen. The antigen PLGA MPs were prepared using a double emulsion (w/o/w) method, lyophilized, and characterized. Next, the ODFs were prepared by combining the biodegradable polymers – Kollidon 90F, Kollidon VA64, and PEG2000 in ethanol to form a gel base. The final vaccine-loaded ODFs were prepared by combining the vaccine MPs with the gel base using a 3D printer.

Results: The yield of MPs was greater than 80%w/w±5 w/w. The characterization assessments revealed the following 1.) size: less than 2µm. 2.) PDI: 0.4±0.1. 3.) Charge: -26.4 mV ±4.609 for H1N1 microparticles and -23.8 mV ± 3.5 for H3N2 microparticles 4.) %EE: 80% to 90% (values are expressed within a range to account for the different MP preparations). The in vitro nitric oxide (NO) released by the DCs upon exposure to the vaccine MPs showed the immunogenicity of the formulation. The in vitro cytotoxicity assessment revealed that the microparticles were non-cytotoxic to cells. The vaccine-loaded ODFs quickly dissolve (less than 5 mins) in artificial saliva to release the vaccine MP. The diameter of the ODFs was measured as 4mm and the surface pH was 7.2. Following in vivo immunization, we found that the Influenza A H1N1-specific serum IgG and IgA levels and Influenza A H3N2-specific serum IgG and IgA increased significantly ($p \leq 0.0001$) compared to the control group. The IgG subtype analyses showed both significantly high levels of serum IgG1 (Th-2/antibody mediated response) and IgG2a (Th-1/cytotoxic mediated response) antibodies specific to both strains ($p \leq 0.01$) reflecting a robust humoral response. Additionally, we found significant antibody levels (IgG and IgA) in the lungs which show mucosal immunity ($p \leq 0.0001$). The study has yielded promising results thus far.

Conclusion: Overall, buccal immunization using ODFs has great potential to cause a fundamental breakthrough in vaccine development, vaccine acceptance, and pandemic preparedness.

Microenvironmental pH-modulated tetrabenazine solid dispersions for improved physicochemical performance

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Background: Pharmaceutical drug development is very limited by the inadequate poor water solubility of over 40% new drug candidates. Solid dispersions (SDs) have been widely challenged to overcome these limitations by converting the stable, low-energy crystalline drug into disordered amorphous state with high-energy. However, the enhanced dissolution of SDs commonly shows "spring -like behaviors via rapid precipitation and recrystallization. Due to the pH dependent behaviors of poorly soluble weakly acidic and basic drugs, incorporating a pH modifier directly into the SDs can create the modulation of microenvironmental pH (pHm) localized around the drug particles upon dissolution process in a parachute manner. The aims of this study were to design pHm-modulated SDs to ameliorate the solubility and permeability of the weakly basic and poorly water-soluble model drug (TBZ) with extremely limited and pH-dependent water solubility.

Method: Optimal binary TBZ-polyvinyl pyrrolidone K30 (PVPK30) (1:2) and ternary TBZ-PVPK30-fumaric acid (1:2:1) SDs were prepared via spray drying. Physicochemical characteristics of SDs were examined and in vitro dissolution was evaluated in 250 mL of pH 6.8 phosphate buffer using USP paddle II method. Permeability was assessed using permeation barrier membrane and PermeaPad via 5-mL Franz diffusion cell.

Results: Powder X-ray diffraction confirmed that TBZ crystals converted to a partial amorphous state in binary SDs and a complete amorphous form in ternary SDs. Consequently, ternary SDs exhibited significantly improved dissolution and permeability compared with TBZ pure drug. Furthermore, ternary SDs dissolution rates at 2 h reached 81.6 %, markedly higher than binary SDs (46.2 %) and pure TBZ (9.7 %) as a result of synergistic pHm modulation. In vitro permeability at 8 h for ternary SDs was greatly improved in comparison with pure TBZ.

Conclusion: These findings suggested that pHm-modulated SDs could provide a versatility to formulate TBZ dosage forms for better patient centricity.

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Effect of polymer concentration on rheology and 3D printing performance of cefixime hydrogels

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Background: Three-dimensional (3D) printing has emerged as a promising technology for the development of personalized pharmaceutical dosage forms, enabling precise control over drug dose, geometry, and release characteristics. Among various printing techniques, semi-solid extrusion requires materials with carefully optimized rheological properties to ensure adequate flow during extrusion and structural stability after deposition. Thermoresponsive polymers such as poloxamer P407 are widely investigated for this purpose due to their gel-forming ability and biocompatibility. Therefore, the aim of this study was to develop and characterize cefixime-loaded poloxamer hydrogels with varying polymer concentrations and to evaluate their rheological behavior and suitability for 3D printing applications.

Method: Five hydrogel formulations (F1–F5) were prepared for 3D printing using a constant amount of distilled water (4 g) as vehicle and cefixime (kindly donated by Alkaloid AD, Skopje, North Macedonia) (0.8 g) as the active ingredient, while varying the concentration of poloxamer P407 (BASF Schweiz AG, Germany) (16-32 %, w/w). Hydrogels were prepared by the cold dispersion method. Rheological properties were determined using a modular compact rheometer (MCR 92, Anton Paar, Austria) by oscillatory amplitude sweep tests. Shear stress, storage modulus, loss modulus, loss factor, torque, and complex viscosity were recorded.
Printability-related performance was evaluated through filament formation, layer stacking, and 3D printing tests using different nozzle diameters (18G, 22G, 25G). Filament integrity (>5 mm), layer definition, and structural stability of 10 × 2 mm cylindrical tablets (5 layers) were visually assessed and classified on a three-point scale (0–2).

Results: All five formulations (F1–F5) demonstrated concentration-dependent rheological behavior. A non-linear increase in shear stress with increasing shear strain was observed, confirming structured gel-like behavior suitable for semi-solid extrusion. Mean shear stress increased above ~25% poloxamer, indicating a critical gel-strength threshold.

Storage modulus, torque, and complex viscosity also increased with polymer concentration, while the loss factor decreased, reflecting a transition from predominantly viscous to more elastic, structured gel systems, with a notable rheological shift around 24–25% poloxamer. Complex viscosity rose from 6.06×10^5 mPa·s (F1) to 1.98×10^6 mPa·s (F4), confirming greater resistance to deformation at higher polymer levels. F3–F5 exhibited higher torque values, indicating improved mechanical stability but potentially increased extrusion resistance.

Filament testing revealed unsuccessful extrusion for F1 due to droplet formation. F2 formed filaments >5 mm but with end-droplet instability. F3 demonstrated optimal filament integrity, particularly through 22G and 25G nozzles (score 2). F4 and F5 produced continuous but slightly curved filaments (score 1), reflecting higher structural rigidity. The printability test using the 22GN nozzle showed increasing polymer concentration improved performance, with F1–F3 scoring 0, F4 scoring 1, and F5 achieving the highest stability (score 2).

Conclusion: Increasing the concentration of poloxamer P407 significantly enhanced the rheological properties, mechanical strength, and printability of cefixime-loaded hydrogels, with a critical gelation threshold observed at approximately 24–25% polymer content. Formulations containing around 25–32% poloxamer (particularly F4 and F5) demonstrated the most favorable balance between structural stability and 3D printing performance, making them suitable candidates for semi-solid extrusion printing.

From bench to clinic: Structural integrity, interaction profile and stability of a new candidate leishmaniasis therapeutic vaccine for phase 1 clinical trials

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Background: Leishmaniasis remains a critical global health challenge, characterized by a limited and toxic therapeutic arsenal. As a strategy to improve clinical outcomes and reduce reliance on systemic chemotherapy, our group has developed VaxLeish, a therapeutic vaccine candidate designed for Clinical Phase 1 trials. The formulation consists of a lyophilized recombinant antigen, and the adjuvant combined at the time of use. Transitioning this candidate from bench to clinic requires a robust characterization of its physicochemical properties and stability, ensuring that the product maintains its critical quality attributes (CQAs) and safety profile under clinical conditions. The aim of this study was to perform the pre-clinical pharmaceutical characterization required to support a Phase 1 clinical trial application. We evaluated the interaction between antigen and adjuvant, and conducted accelerated and long-term stability assays. These analyses aimed to establish the vaccine's shelf life, ensure batch-to-batch consistency, and guarantee that the structural integrity and immunogenic potential of the formulation remain stable for safe administration in humans.

Method: Physicochemical characterization and formulation stability were evaluated through a multiparametric analytical approach. Particle size distribution and polydispersity index (PdI) were determined by Dynamic Light Scattering (DLS). Colloidal stability and particle surface charge were determined by Zeta Potential through electrophoretic mobility, to understand the electrostatic nature of the interaction. The association efficiency was monitored by SDS-PAGE and Western Blot (WB) using specific antibodies. Transmission electron microscopy (TEM) was used to visualize the morphology, homogeneity, and interaction between antigen and adjuvant fibers. The conformational integrity of antigen was monitored by Circular Dichroism (CD) to assess secondary structure, and by Fluorescence Spectroscopy, utilizing intrinsic tyrosine emission to detect potential changes in the tertiary structure. To evaluate the influence of the antigen-adjuvant interaction on the biological response, an immunogenicity assay was performed in an animal model. Animals were divided into experimental groups to compare the administration of the VaxLeish previously associated via reconstitution versus the concomitant administration of the isolated antigen and adjuvant. Stability assays followed the guidelines established in resolution of the collegiate board (RDC) 412 to identify potential protein aggregation or degradation processes over time.

Results: Characterization of VaxLeish demonstrated a physical interaction between antigen and adjuvant, evidenced by a reduction in adjuvant particle size; supression of intrinsic tyrosine fluorescence, and direct visualization via TEM, which revealed antigen particles anchored to the adjuvant's fibrillar. Western Blot assays under non-denaturing conditions confirmed the formation of high molecular weight complexes. However, circular dichroism and fluorescence analyses indicated that antigen secondary and tertiary structures were preserved. The influence of this interaction on the biological response was evaluated in an animal model. Immunogenicity was similar in both groups, indicating a consistent immune response in the pre-association and the separate administration of the antigen and adjuvant. Furthermore, stability studies showed that the lyophilized formulation remained within specifications for 6 months under accelerated conditions and for 9 months under long-term storage.

Conclusion: The antigen-adjuvant interaction is biophysically mild, preserving the structural identity and immunogenic potential. The formulation exhibits robust stability, supporting its potential for clinical application.

Wound dressings based on Carob Gum and Pistacia atlantica: Development and in vitro physicochemical and structural characterization

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Background: Chronic wound management remains a significant clinical challenge, since chronic wounds can eventually become fatal. Natural polysaccharide-based wound dressings have attracted attention due to their biodegradability and biocompatibility. Plant-derived bioactive compounds are being explored for wound healing applications due to their antimicrobial, antioxidant, and anti-inflammatory properties. Ceratonia siliqua (Carob) and Pistacia atlantica (PA) have been traditionally used in herbal medicine for treating skin injuries and wounds, and recent studies suggest that its bioactive compounds could support the wound healing process.

Purpose: In this study, wound dressing systems based on locust bean gum and Pistacia atlantica were developed and characterized to evaluate their physicochemical and structural properties in vitro.

Method: Aqueous solutions of carob gum (LBG) and PA were prepared by dissolving each components in various concentrations in distilled water at 80-90 °C for 30 min and acetic acid, respectively. Various polymer concentrations (2 - 4%) and polymer ratios (0:1, 1:0, 1:1, 2:1) were chosen. Afterwards, the solutions were mixed until complete dissolution and poured into glass petri-dishes, following by incubation at -20 °C for 24 h. Subsequently, the samples were lyophilized leading to cryogels. Citric acid was chosen as functional additive. The dressings were assessed for their morphology and porosity and swelling ability as well as water retention ratio and moisture loss. Fourier-transform infrared spectroscopy (FTIR) was performed to investigate potential interactions between components. In vitro biocompatibility and antimicrobial studies against Staphylococcus aureus were also conducted.

Results: The LBG/PA sponges displayed a porous structure with porosity values between 61% and 76% depending on different polymer concentrations and formulation ratios. The results of FTIR spectroscopy did not show any specific interactions between the components as no new peaks or significant shifts were revealed. The moisture loss after 24 h ranged from 7% to 29% indicating moderate water loss. The sponges displayed high swelling capacity (973- 2718%) after 15 minutes followed by a slow reduction because of dissolution. The water retention ratio values showed a slow decline during the 24-h period which demonstrated that wound dressings can retent water. The developed sponges demonstrated excellent biocompatibility but they displayed only minimal antimicrobial effectiveness against Staphylococcus aureus.

Conclusion: According to the findings, Carob gum-Pistacia atlantica-based dressings maintain their structural integrity and physicochemical suitability and compatibility. The developed LBG/PA sponges exhibited high porosity along with efficient swelling ability and water retention, indicating effective fluid uptake and suitability for wound exudate management. The sponges also demonstrated improved biocompatibility, but their antimicrobial effectiveness against Staphylococcus aureus remained limited. Overall, the developed porous matrices show promising potential for wound dressing applications. Future studies will examine the use bioactive plant extracts, such as Asphodelus ramosus and Ceratonia siliqua leaf extracts could further enhance the antimicrobial and therapeutic properties of the developed wound dressing materials.

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Intelligent monitoring and control of tablet coating processes based on near-infrared spectroscopy

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Background: Tablet coating is a critical unit operation in solid dosage form manufacturing, significantly influencing tablet appearance, mechanical stability, moisture protection and drug release behaviour. Coating thickness is recognised as a critical quality attribute (CQA) and requires precise regulation to ensure product consistency. Conventional offline measurements, including gravimetric and microscopic methods, are destructive and time-consuming, preventing real-time monitoring and proactive process control. The implementation of Process Analytical Technology (PAT) and Quality by Design (QbD) frameworks emphasises continuous monitoring of CQAs and dynamic regulation of critical process parameters (CPPs). Near-infrared spectroscopy (NIRS), operating within the 780–2500 nm spectral region, provides rapid, non-destructive and in-line analytical capability. However, integration of quantitative spectral modelling with closed-loop feedback control for active thickness regulation remains limited. This study aimed to establish an intelligent in-line monitoring and dynamic control system for tablet coating thickness based on NIRS and proportional–integral–derivative (PID) control.

Method: A three-factor, three-level Box–Behnken experimental design was employed to investigate the effects of spray pressure, inlet air temperature and spray gun distance on coating thickness. Statistical modelling identified significant factors and interactions to optimise process conditions. Under optimised parameters, eleven independent coating batches were produced. In-line NIR spectra were continuously collected using a miniature spectrometer in diffuse reflectance mode. Reference coating thickness values were determined using a validated volumetric differential method combined with ultraviolet quantification of a fluorescent tracer. Spectral data were pre-processed using standard normal variate transformation, Savitzky–Golay smoothing and normalisation. Variable selection was performed using competitive adaptive reweighted sampling (CARS). A partial least squares (PLS) regression model was developed and evaluated using the coefficient of determination (R^2), root mean square error of prediction (RMSEP) and residual predictive deviation (RPD). The optimised PLS model was integrated with a PID controller to enable real-time closed-loop regulation of coating thickness via automatic adjustment of spray rate.

Results: Experimental design analysis demonstrated that inlet air temperature and spray gun distance exerted significant negative effects on coating thickness, with a notable interaction between the two parameters. The optimal process conditions were determined as 0.8 bar spray pressure, 44 °C inlet air temperature and 15 cm spray gun distance. The final PLS model achieved strong predictive performance on an independent test set (R^2 = 0.9078, RMSEP = 9.8133 µm, RPD = 2.3211), indicating reliable quantitative capability. Field validation confirmed high consistency between predicted and measured thickness values. Integration of the PID control strategy enabled automatic correction of deviations under simulated abnormal conditions, including sudden increases or decreases in spray rate. Closed-loop operation effectively restored thickness within predefined control limits and improved process stability.

Conclusion: This study demonstrates the feasibility of integrating NIRS-based quantitative modelling with PID feedback control to achieve real-time monitoring and autonomous regulation of tablet coating thickness. The proposed system enhances process robustness, reduces variability and supports intelligent pharmaceutical manufacturing within the PAT and QbD frameworks. The findings provide practical guidance for advancing data-driven and closed-loop control strategies in solid dosage production.

Pharmacological effects of P1075 and NS1619 on human saphenous veins obtained from patients with type-2 diabetes mellitus

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Background: Potassium channel openers (PCOs) constitute a heterogeneous group of compounds characterized by their capacity to activate potassium (K) channels. Activation of these channels in vascular smooth muscle cells produces membrane hyperpolarization, leading to subsequent vasorelaxation. In addition to well-established PCOs such as nicorandil, diazoxide, and pinacidil, newly developed agents have demonstrated increased pharmacological potency. Among these compounds, P1075 is recognized as a potent activator of ATP-sensitive potassium (KATP) channels, whereas NS1619 acts primarily as an opener of large-conductance calcium-activated potassium (BKCa) channels.

Purpose: The objective of the present study was to evaluate and compare their pharmacological efficacy in inducing vasorelaxation in human saphenous veins (HSV) obtained from patients with type-2 diabetes mellitus (T2DM).

Method: Endothelium-denuded HSV rings obtained from patients undergoing bypass surgery were mounted in an organ bath system, and isometric tension was recorded. HSV segments were precontracted with phenylephrine (100 µM), followed by cumulative administration of P1075 (0.001–100 µM) or NS1619 (0.001–100 µM). Selective blockers of KATP and BKCa channels, glibenclamide (GLB, 10 µM) and iberiotoxin (IbTx, 0.1 µM), respectively, were used in separate experimental series. Data are expressed as mean ± standard error of the mean (SEM).

Results: P1075 and NS1619 induced concentration-dependent vasorelaxation in diabetic HSV (pD2 = 6.45 ± 0.40, n = 6 and pD2 = 3.98 ± 0.95, n = 6, respectively). GLB significantly antagonized the effects of P1075 in HSV obtained from T2DM patients (pD2 = 3.76 ± 0.63, n = 6, $P < 0.01$). In contrast, IbTx not only failed to antagonize NS1619-induced responses in diabetic HSV but also enhanced its vasorelaxant effect (pD2 = 6.13 ± 0.51, n = 7, $P > 0.05$).

Conclusion: P1075, a synthetic analogue of pinacidil with high pharmacological potency, further substantiates its role as a selective activator of KATP channels in diabetic HSV preparations. In contrast, our experimental findings did not confirm NS1619 as a specific BKCa channel activator, suggesting that BKCa channel function in diabetic HSV may be impaired or functionally altered under diabetic conditions.

Enhancing extracellular vesicle secretion from antigen-presenting cells via antigen-loaded and calcium-incorporated chitosan nanoparticles

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Background: Extracellular vesicles (EVs) are cell-originated lipid membrane vesicles secreted by cells to extracellular space. They play an important role in intercellular communication and have been recognized as a safe drug delivery platform. Dendritic cell-derived EVs (DC-EVs) and macrophage-derived EVs (M-EVs) have been identified as potential immunomodulatory adjuvants in cancer immunotherapy. However, one of the limitations of using EVs as therapeutic agents or drug carriers is the low yields of EVs from cell culture medium under standard condition. Intracellular calcium content has been identified as a key factor influencing the EV generation and secretion. Therefore, the methods that can enhance intracellular calcium level will be a good strategy for EV secretion. In this study, chitosan-based nanoparticles (CS NPs) and ovalbumin (OVA) were used as a carrier and model antigen. To further enhance the antigen cross-presentation and EV secretion by antigen-presenting cells, calcium ions were incorporated into our CS NPs (Ca-CS NPs).

Method: CS NPs were prepared via ionic gelation method, followed by electrostatic interactions with OVA and calcium ions to form Ca-CS-OVA NPs. Different concentrations of calcium ions (1Ca = 1 mM $CaCl_2$; 5Ca = 5 mM $CaCl_2$; 10Ca = 10 mM $CaCl_2$) were incorporated into CS solution to investigate their effects on nanoparticle properties. NPs were characterized and evaluated for cytotoxicity, antigen cross-presentation, dendritic cell (DC) maturation and EV secretion in vitro. EVs were isolated via ultrafiltration and further characterized using transmission electron microscopy (TEM).

Results: The presence of calcium chloride influenced the size, zeta-potential and loading efficiency of CS NPs. Calcium incorporation increased the surface charge and antigen loading efficiency of NPs. However, excessive calcium incorporation led to increasing the size of NPs. The reduced zeta-potential observed after OVA loading further confirmed the successful adsorption of OVA onto the nanoparticle surface. Ca-CS-OVA NPs enhanced antigen cross-presentation in DC2.4 cells and promoted maturation of bone marrow-derived dendritic cells (BMDCs). Quantification of total protein and acetylcholinesterase activity indicated that Ca-CS NPs increased EV secretion. Moreover, the formulations did not significantly reduce the viability of DC2.4 and RAW264.7 cells after 24 h of incubation, suggesting that the observed EVs were not derived from death cells.

Conclusion: The physicochemical properties of Ca-CS NPs were favorable for cellular uptake. Ca-CS NPs enhanced maturation and antigen cross-presentation in DC2.4 and BMDCs. In addition, Ca-CS NPs promoted EV secretion and without inducing cytotoxicity in DC2.4 and RAW264.7 cells. Overall, Ca-CS NPs represent a promising, easy-prepared and safe platform for antigen delivery and EV secretion.

Cellulose nanocrystals derived from brewery spent grain as a binder in diclofenac tablets

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Background: The brewing industry generates millions of tons of brewery spent grain (BSG) annually, posing environmental challenges if not properly managed. Utilizing BSG for the isolation of cellulose microfiber (CMF) provides a sustainable solution by reducing waste disposal costs, lowering pharmaceutical production expenses, and minimizing environmental pollution. BSG is a lignocellulosic byproduct rich in cellulose, hemicellulose, and lignin, making it a valuable raw material for producing functional biomaterials through bioprocessing.
Cellulose microfiber possesses physicochemical properties comparable to Avicel and has potential pharmaceutical applications as a tablet binder due to its compressibility, flowability, and binding properties. Therefore, this study aimed to isolate CMF from BSG using acid hydrolysis, characterize the material, and evaluate its suitability as a binder in Diclofenac sodium tablet formulation.

Method: Cellulose microfiber was isolated from brewery spent grain using an acid hydrolysis method following pretreatment steps to remove non-cellulosic components. The isolated cellulose was evaluated through organoleptic, physicochemical, and phytochemical analyses to determine its purity and basic characteristics. Further characterization was performed using Fourier Transform Infrared Spectroscopy (FTIR) for functional group identification, Differential Scanning Calorimetry (DSC) for thermal analysis, Atomic Absorption Spectroscopy (AAS) for metal content determination, Scanning Electron Microscopy (SEM) for surface morphology, and X-ray Diffraction (XRD) for crystallinity assessment.
The isolated cellulose microfiber was used as a binder in tablets containing 50 mg of Diclofenac sodium. Powder flow properties of blends containing CMF and Avicel were evaluated using bulk density, tapped density, and true density measurements, from which Hausner's ratio and Carr's compressibility index were calculated. Tablets were prepared by the direct compression method using varying binder concentrations.

Results: SEM analysis showed that CMF consisted of rough, elongated fibrous structures with particle sizes ranging from 10.7–26.3 µm, whereas Avicel exhibited irregular compact particles with larger sizes ranging from 34–60.3 µm. XRD analysis revealed crystallinity indices of 63.33% for BSG-derived cellulose and 81.57% for Avicel, indicating a higher amorphous content in CMF. FTIR spectra confirmed characteristic cellulose absorption bands similar to Avicel. AAS analysis detected trace metals including Na, Ca, K, Mg, Fe, Mn, Cu, Ni, and Zn, while phytochemical screening revealed phenols, flavonoids, saponins, tannins, and alkaloids. DSC results showed that both CMF and Avicel were thermally stable.
Flow property evaluation indicated poorer flowability for CMF. Despite poorer flow, CMF produced tablets with higher hardness (5.18 kgF) than Avicel tablets (4.20 kgF). Friability values were within acceptable limits, with CMF tablets showing slightly lower friability (0.71%) than Avicel tablets (0.81%). Tablet disintegration was faster for Avicel (0.67 min) than CMF (0.99 min). Dissolution studies showed nearly complete drug release from Avicel tablets within 60 minutes, while CMF tablets released approximately 92% within the same period.

Conclusion: Cellulose microfiber derived from BSG demonstrated suitable physicochemical and mechanical properties for use as a pharmaceutical tablet binder. Although it exhibited poorer powder flow than Avicel, it produced stronger tablets with acceptable friability and satisfactory drug release, indicating its potential as a sustainable alternative excipient derived from brewery spent grain.

Stability of two 6-mg/mL topiramate formulations in a new paraben- and sugar-free suspension vehicle

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Background: Even when a drug is approved for a pediatric indication, manufacturers are under no obligation to market a child-friendly formulation. This gap is well recognized by regulatory agencies and, consequently, access to these treatments often relies on the compounding of oral liquid formulations. One example of this gap is topiramate, a drug approved for the management of epilepsy in both children and adults. In absence of a commercially-available liquid dosage form, compounding remains the best alternative to give pediatrics access to this treatment. Because long-term

therapy with antiepileptic is common, having access to stability data for topiramate in a suspension vehicle free from potentially harmful excipients would be beneficial.

The purpose of this study was to assess the stability of two topiramate 6-mg/mL compounded preparations in a new paraben- and sugar-free suspension vehicle. The formulations were prepared either from topiramate bulk powder or commercial 100-mg tablets and studied for 90 days in amber polyethylene terephthalate (PET) plastic bottles and 30 days in oral amber polypropylene (PP) plastic syringes at 25±2°C/60±5% relative humidity (RH). Additionally, the impact of potential temperature excursions on formulation stability was assessed by exposing them to three 24-hours cycles either at -20±5°C or 40±2°C/75±5% RH, before returning to 25±2°C/60±5% RH until the end of the study.

Method: Three batches of both topiramate formulations were prepared and studied under the prescribed storage conditions. At predetermined timepoints, chemical stability of topiramate was evaluated using a validated stability-indicating high-pressure liquid chromatography coupled to ultraviolet detector (HPLC-UV) method along with pH measurements. Physical properties, such as appearance, color and homogeneity, were evaluated visually at each timepoint. Stability was defined as the ability of the formulation to retain ±10.0% of its initial concentration, no change of more than 1.0 pH unit, and no notable change in physical properties. The preservative system efficacy of each formulation was evaluated at the beginning and at the end of the study using the USP <51> Antimicrobial Effectiveness Test (AET) to support the assigned beyond-use date (BUD).

Results: No visual changes were observed under all storage conditions over the entire stability study. The mean concentration of each formulation remained at all timepoints between ±4.0% of their respective initial concentration. The pH of both formulations was initially at 4.5 and remained at ±0.1 pH unit at each timepoint. Preservative efficacy of both topiramate formulations conformed to USP <51> specifications for all prescribed microbiological strains even after 90 days of storage at 25±2°C/60±5% RH in amber PET bottles.

Conclusion: Chemical, physical and microbiological stability results support the assignment of a 90 days BUD when stored in amber PET bottles and 30 days in amber oral PP syringes at room temperature for 6 mg/mL topiramate compounded formulations prepared either from bulk powder or tablets in a new paraben- and sugar-free suspension vehicle. Temperature excursion data will assist clinicians by reducing uncertainty when managing stability during transportation and patient daily use.

Perceived rapid-onset warming from a non-medicated thermosensory emulgel: Expert sensory profiling and an independent exploratory study with user evaluation

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Background: Non-medicated thermosensory products are widely used in self-care, and pharmacists are often consulted about expected onset and sensory characteristics. Sensory properties can influence acceptability and contribute to the overall user experience, yet empirical descriptions of perceived warming experience over time from topical formulations are limited. The onset, intensity, and temporal profile of perceived warming from a non-medicated thermosensory emulgel, applied on skin for soothing and moisturizing, were assessed using an expert sensory panel (study 1), and an independent user-perceived warming evaluation in an exploratory cosmetic study (study 2).

Method: An adapted quantitative descriptive analysis (Study 1) was conducted with 11 trained sensory panellists under blinded conditions. Perceived warming intensity was rated on a 0–100 scale for four application regimens: 1 g, 2 g, 4 g (single application), and 4×1 g applied at 0, 10, 20, and 30 minutes. Regimens were evaluated on three anatomical sites (shoulder, lower-back, calf) with ratings recorded at predefined intervals over 60 minutes (duplicate assessments). Analyses used ANOVA with a 95% confidence level. In an exploratory cosmetic study (study 2), healthy adults (n=12) received a single 2 g application to the left neck and shoulder area and rated warming sensation on a six-point scale (-1 to 4) at baseline and at 2, 5-, 10-, 15- and 20-minutes post-application; results were summarized descriptively.

Results: Panellists (study 1) reported increased perceived warming within 2 minutes across regimens and sites following application of the non-medicated thermosensory emulgel. Perceived warming intensity showed a nonlinear relationship with quantity. Compared with 1 g, 2 g produced higher perceived warming, with separation evident at approximately 3 minutes (shoulder), 5 minutes (calf), and 7 minutes (lower-back); peak perceived intensity with 2 g was about one-third higher than with 1 g. Perceived warming was generally higher with 4 g than 2 g, although no early-phase difference (≤10 minutes) was observed on the shoulder, and the incremental increase from 2 g to 4 g was smaller than that from 1 g to 2 g. The 4×1 g regimen showed a slower, more sustained increase, with a later peak over 60 minutes, whereas single application regimens peaked at approximately 16 minutes before declining. Peak values (0–100) were 34.9/42.6/50.4/47.2 (lower back) and 18.0/23.2/31.5/29.9 (calf) for 1 g/2 g/4 g/4×1 g; on the shoulder, peak values were ~30.2 (1 g) and ~46.0 for ≥2 g regimens. In the exploratory study (study 2),

participants reported warming at 2 minutes post-application and at subsequent timepoints (up to 20 minutes), consistent with panel observations.

Conclusion: Expert sensory profiling as well as an exploratory study showed rapid-onset of perceived warming and sustained warming sensation following application on skin of a non-medicated soothing and moisturizing thermosensory emulgel. Differences in intensity and temporal pattern across quantities and sites indicate that perceived warming varies with application conditions. These descriptive findings may support pharmacists in evidence-informed counselling on thermosensory products by setting expectations for onset and sensory intensity. Further research is warranted to confirm these findings and assess applicability in broader contexts.

Comparative assessment of intranasal deposition patterns between two nasal spray pump designs: Findings from a nasal cast study

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Background: Optimal intranasal drug delivery is essential in community and self-care settings, where pharmacists frequently advise on correct nasal spray use. Device mechanics, including nozzle geometry, pump design, and plume characteristics, can influence deposition across key nasal regions and may affect therapeutic performance and user experience. In vitro nasal cast models offer a controlled and anatomically representative platform for quantifying deposition patterns and comparing device-related performance under standardised conditions. However, comparative data remain limited. This study compared two nasal spray pump designs to evaluate how device factors influence intranasal disposition patterns relevant to real-world use.

Method: This investigation compared two nasal spray designs: a fine-mist spray and a regular pump with no-drip formula, both containing oxymetazoline hydrochloride 0.05% using a validated Koken nasal cast under controlled conditions. Each spray was actuated into the right nostril with the cast upright, the nozzle inserted ~10 mm and angled 45° outward to reflect typical user technique. Ten units per spray were tested (one actuation each). Deposition images were captured and quantified using pixel-to-area conversion calibrated against a 1 cm^2 reference marker to calculate deposition area (cm^2). Shot weights were recorded, and deposition values were normalised to account for dose-volume differences. Regional coverage across nasal structures was assessed qualitatively through visual inspection of deposition patterns.

Results: Fine-mist spray produced a significantly larger mean deposition area (7.03 cm^2) than regular pump with no-drip formula (4.00 cm^2) and extended deeper into the superior, middle and inferior turbinate regions ($p < 0.0001$). Although fine-mist spray exhibited a higher shot weight (141.7 mg versus 101.4 mg), normalised deposition analysis adjusting for delivered volume continued to show a significant difference ($p = 0.0003$). Qualitatively, the fine-mist pump showed more extensive coverage across inferior, middle, and superior turbinates with deposition extending deeper toward the olfactory region.

Conclusion: This study demonstrates that nasal spray pump design affects intranasal deposition patterns under controlled in vitro conditions, with the fine-mist spray achieving broader and deeper coverage than regular pump with no-drip formula. These findings underline the influence of device mechanics on deposition behaviour and may support pharmacists in advising on nasal spray use. Further research is needed to explore user-dependent factors and to determine whether in vitro deposition differences correspond to perceptible or clinical benefits.

Intravaginal fosfomycin pessaries for bacterial vaginosis: A translational preclinical evaluation of enhanced local antibiotic delivery

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Background: Bacterial vaginosis (BV) affects a significant women population worldwide. It is associated with recurrence rates exceeding 50% within one year. Standard oral therapies often provide suboptimal vaginal drug exposure and may contribute to systemic adverse effects and antimicrobial resistance. Localized antibiotic delivery may improve therapeutic outcomes. Based on this we evaluated the translational potential of an intravaginal fosfomycin tromethamine pessary as a targeted alternative to oral therapy.

Method: A lipid-based mucoadhesive fosfomycin pessary was formulated and evaluated for physicochemical stability, liquefaction time, mechanical strength, and in vitro release kinetics. Comparative pharmacokinetic profiling was carried out in female rabbits following intravaginal pessary versus oral suspension administration. Antibacterial efficacy was

evaluated in an induced vaginal Escherichia coli infection model. Vaginal tissue was assessed for any histological changes.

Results: The optimized pessary demonstrated acceptable physicochemical characteristics that sustained in vitro drug release. Intravaginal administration resulted in approximately two-fold greater systemic exposure and earlier peak concentration compared with oral suspension. The in vivo analysis indicated pessary formulation achieved significantly greater ($p < 0.01$) bacterial reduction. Histopathological evaluation confirmed preservation of vaginal mucosal integrity without inflammatory indications.

Conclusion: Targeted intravaginal delivery of fosfomycin enhances pharmacokinetic exposure and antibacterial efficacy while maintaining local tissue safety. This preclinical evidence supports further clinical development of vaginal fosfomycin therapy as a strategy to improve treatment outcomes and reduce recurrence in bacterial vaginosis.

Administering risperidone oral solution mixed with black tea to rats does not reduce the area under the blood concentration-time curve of risperidone

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Background: Risperidone oral solution (RIS-OS), a schizophrenia medication, is an easy-to-take formulation that enhances medication adherence and has rapid-onset efficacy. However, there are restriction regarding its administration. For example, mixing with beverages such as black tea is prohibited, as this is associated with reductions in RIS content. Although we have previously established that a proportion of outpatients in Japan mix RIS-OS with beverages for administration, there is currently no pharmacokinetic information available for RIS-OS when administered mixed with black tea. In this study, using rats, we aimed to clarify the pharmacokinetic parameters of RIS and its active metabolite 9-OH-RIS following administration of RIS-OS mixed with black tea.

Method: Male Wistar rats aged 8 weeks were assigned to one of two oral administration groups (3 rats/group): administration after mixing RIS-OS with water and administration after mixing RIS-OS with Dimbula tea. The RIS dosage was set at 1.25 mg/kg, and following dilution with water/tea, the concentration of the solution was approximately 0.091 mg/mL. Blood samples were collected from the tail vein using DBS collection paper at nine time points: 5, 10, 15, 30, 60, 120, 180, 240, and 360 min post-administration. Collected samples were eluted and quantitatively analysed for RIS and 9-OH-RIS using HPLC/ESI-MS/MS

Results: With respect to the blood concentration profiles of RIS and 9-OH-RIS, whereas rats in the water mixture group had higher concentrations up to 60 min post-administration, after 120 min, we detected higher concentrations among rats in the black tea mixture group. In terms of the pharmacokinetic parameters of RIS, compared with the water mixture group, we detected a significantly lower maximum whole blood concentration among rats administered the black tea mixture, whereas there were no significant between-group differences regarding the elimination rate constant (kel) or the area under the blood concentration-time curve (AUC). However, similar to findings for 9-OH-RIS, we observed significantly higher values for the area under the moment curve and mean residence time (MRT) for the black tea mixture group.

Conclusion: A novel finding of this study is that RIS, for which we have observed a reduction in content in vitro when mixed with black tea, showed no significant difference from that mixed with water with respect to the AUC in vivo. Among rats in the black tea mixture group, kel remained unchanged, whereas MRT was prolonged, indicating that the physicochemical properties of RIS within the digestive tract lumen may have resulted in an absorption process distinct from that of RIS mixed with water. With respect to the mechanisms whereby mixing RIS with black tea reduces RIS content, it is believed that a certain component in RIS forms a complex with a black tea component(s), although the identities of these constituents have yet to be clearly established. Notably, in this study, we used only a single type of black tea, and accordingly anticipate that assessments based on analyses of different types of tea will contribute to identifying the constituents associated with the observed reductions in RIS content, and thereby provide relevant pharmaceutical information for RIS-OS.

Locust bean gum - based dressings for wound healing potential: Effect of sodium alginate as an additive on physicochemical properties and biological properties

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Background: Wound healing is a dynamic and complex process which depends on various factors. Therefore, multifunctional wound dressings based on biomaterials which can maintain a moist environment, while providing structural integrity and antimcrobial properties can support tissue regeneration. Natural polysaccharides are promising biomaterials due to their biocompatibility, biodegradability and ease functionalization. Locust bean gum (LBG), a galactomannan polymer, is an emerging biomaterial which can be applied as thickening agent with various biomedical applications.
Purpose: In this study, LBG-based dressings were developed and the effect of sodium alginate as a structural additive on their physicochemical and biological properties was evaluated.

Method: The sponges were fabricated using freeze-drying method; more specifically, aqueous solutions of SA and LBG were prepared at ratios of 100:0, 0:100, 50:50, 25:75, and 75:25. Citric acid was incorporated as an additive into the polymeric dressings, to enhance their mechanical strength and functional performance. After its addition into the polymeric solutions, stirring until complete homogenization followed by. The resulting solutions were subsequently frozen and lyophilized to produce a porous sponge dressing. Fourier-transform infrared spectroscopy (FTIR) was used to investigate potential interactions between compontents.Additionally, the sponges were characterized for their physicochemical and functional properties. Morphology, porosity, swelling ability, in vitro cell biocompatibility on HaCaT cells and antimicrobial capacity were evaluated.

Results: According to the macroscopic analysis of the wound dressings, the sponges showed a hihly porous interconnected system with porosity ranged from 30-50%, revealing that the polymer ratio has a key role in their porous structure. FTIR spectra demonstrated similar characteristic absorption bands as of the corresponding pure polymers. In addition, the sponges demonstrated immediate swelling and followed by rapid hydrolytic degradation in simulated wound fluid. Furthermore, the dressings had satisfactory antimicrobial activity against Staphylococcus aureus which was dependent to the SA ratio. Moreover, in vitro biocompatibility studies depicted that the developed sponges showed good cytocompatibility toward HaCaT keratinocytes, with cell viability values above 80% at most tested concentrations and time points. The SA/LBG-based dressings demonstrate keratinocyte survival enabling, while they potentially enhance cellular processes that promote wound repair.

Conclusion: It was demonstrated that by modifying the polymer ratio, it is possible to improve the structure and functionality of the dressings and improve its overall performance. The developed sponges can act as promising materials for wound healing applications. The incorporation of sodium alginate improved matrix stability and hydration behavior while maintaining favorable biocompatibility. Furthermore, the formulations demonstrated improved antimicrobial effect and in vitro biocompatibility on keratinocytes, supporting their potential role in wound healing. Overall, sodium alginate can be added as additive within the LBG-based system, enhancing physicochemical characteristics and contributing to improved overal potential.

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Cellulose nanocrystal stabilised pickering emulgels for sustained colonic delivery of budesonide

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Background: Inflammatory bowel disease (IBD) is a chronic gastrointestinal condition that could benefit from targeted drug delivery strategies to minimise systemic side effects.

Conventional therapies often limited by poor drug solubility and a lack of site specificity, reducing their effectiveness. To overcome these challenges, novel drug delivery systems are being designed to enable localised and effective delivery to sites of intestinal inflammation while minimising systemic exposure and adverse effects.

Emulgels are a hybrid material that combines an oil-in-water emulsion with a gel in the continuous phase, imparting "gel-like" properties to the emulsion. This system offers several advantages for drug delivery, including the ability to solubilise both hydrophilic and hydrophobic drugs, controlled release of active compound, improved stability and storage, prolonged retention time, and enhanced drug-loading efficiency.

This study introduces emulgels based on Pickering emulsions stabilised by cellulose nanocrystals (CNCs) and reinforced with a supramolecular gel phase, which is based on host-guest interactions between α-cyclodextrin (α-CD) and polyethylene glycol (PEG). These emulgels were explored as a novel platform for the local delivery of budesonide to the gastrointestinal tract.

Method: CNC-stabilised Pickering emulsions (40–70% v/v oil, 0.5–2 mg·mL^{-1} CNC) were characterised for droplet size, zeta potential, stability, and rheology. Emulgels were obtained by incorporating α-CD (6–10% w/v) and PEG (5–10% w/v, 10 and 20 kg/mol) in the aqueous phase. The emulgels were assessed for long-term stability, rheological properties, and drug release profile. Mucoadhesion was assessed using porcine intestinal tissue. Cytocompatibility was evaluated using an MTS assay, and epithelial integrity was monitored using transepithelial electrical resistance (TEER). The permeability of budesonide was determined across Caco-2 cell monolayers cultured in Transwell™ inserts.

Results: Pickering emulsions showed enhanced stability with increasing CNC concentration and oil volume fraction. Incorporating a gel phase of α-CD/PEG markedly increased the storage modulus, G', up to 1.53×10^5 Pa (70% v/v oil, 5%w/vPEG 10 or 20 kg/mol, and 10%w/v α-CD) without phase separation over 30 days, indicating long-term stability.

The emulgels display a shear-thinning behaviour and quickly recovered after release of the strain, equally after injection through a syringe. Mucoadhesiveness was significantly improved in 70% oil formulations, particularly with 5% PEG (10 kg/mol) and 10% α-CD, compared with PEG solution alone ($p < 0.05$) when tested on porcine intestinal tissue.

Budesonide was efficiently loaded (86–98%) and released in a sustained manner over 72 hours. Permeation studies confirmed epithelial budesonide transport with an apparent permeability coefficient (Papp) of 3.22 × 10^{-6} cm·s-1, compared with 7.96 × 10^{-6} cm·s-1 for budesonide solution, indicating reduced relative to solution ($p < 0.05$). The emulgels did not compromise epithelial barrier integrity and were non-toxic to Caco-2 cells.

Conclusion: CNC-stabilised Pickering emulgels with α-CD/PEG demonstrate high stability, injectability, biocompatibility, mucoadhesion, and controlled drug release, making them promising candidates for localised IBD therapy.

Study on the effect of soluble microneedle-loaded siPCSK9 mesenchymal stem cell biomimetic vesicles in improving psoriasis lesions

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Background: Psoriasis is a chronic inflammatory skin disease involving keratinocyte hyperproliferation and immune dysregulation. Although biologics have advanced treatment, targeting "undruggable" molecules remains challenging. RNA interference offers a strategy to silence pathogenic genes post-transcriptionally. Proprotein convertase subtilisin/kexin type 9 (PCSK9) has been implicated in psoriasis pathogenesis beyond its role in lipid metabolism, promoting keratinocyte proliferation and inflammation. However, efficient delivery of PCSK9 siRNA (siPCSK9) is hindered by the stratum corneum and RNA instability.

Objective: To construct a dissolvable microneedle (MN) system loaded with mesenchymal stem cell-derived biomimetic nanovesicles carrying siPCSK9 (MN-MSCNV@siPCSK9) and evaluate its therapeutic efficacy in psoriasis.

Method: MSCNVs were prepared by extrusion and loaded with siPCSK9 via electroporation, then incorporated into dissolvable MNs. The system was characterized for size, zeta potential, morphology, protein homology, stability, and encapsulation efficiency. Transdermal delivery was assessed in vitro and in vivo. Therapeutic effects were evaluated in M5-stimulated keratinocytes and imiquimod-induced psoriatic mice using histology, immunohistochemistry, flow cytometry, and qRT-PCR. Biosafety was assessed via histopathology and serum biochemistry.

Results: MSCNV@siPCSK9 showed intact structure, good stability, and protein homology to parent stem cells. The MN system enabled efficient skin penetration and delivery. It reduced M5-induced keratinocyte hyperproliferation and inflammation. In vivo, MN-MSCNV@siPCSK9 decreased epidermal thickness, Ki67, IL-17, and NF-κB activation, restored immune homeostasis, and showed no systemic toxicity.

Conclusion: MN-MSCNV@siPCSK9 offers a minimally invasive, targeted siRNA delivery platform, validating PCSK9 as a therapeutic target in psoriasis and providing a strategy

for treating "undruggable" targets in inflammatory skin diseases.

Study on the effect and mechanism of Xanthatin nanomedicine on breast cancer

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Background: Breast cancer is characterized by high metastasis and recurrence rates, which often cause adverse reactions and drug resistance during radiotherapy and chemotherapy. Xanthatin (Xa), as the main active component of Xanthium from Asteraceae, has a clear inhibitory effect on gastric cancer, lung cancer, colon cancer and other tumors. However, there are problems such as poor water solubility and low bioavailability, which will increase the risk of toxicity. Purpuse: In order to more accurately and effectively play the effect of Xanthatin, the present study combined with nanotechnology was used to provide a new targeted therapy for breast cancer.

Method: The targeting group cRGDfk (cRGD) was modified on the surface of Xa with high efficiency, and then encapsulated into the nano-carrier DSPE-PEG2000 to self-assemble into cRGD-NPs. The molecular structure of the drug was determined by nuclear magnetic resonance spectroscopy, the morphology of the nanoparticles was observed by transmission electron microscopy, and the particle size was determined by dynamic light scattering. The effect of cRGD-Xa on the viability of 4T1 cells was evaluated by MTT cytotoxicity assay. The expression of apoptosis-related proteins was analyzed by Western blot (WB). In vivo, a subcutaneous ectopic breast cancer mouse model was established, and the biodistribution of cRGD-Xa NPs@ICG in the mice was monitored by chemiluminescence imaging. An orthotopic BALB/c nud nude mouse model of breast cancer was established, and the anti-tumor effect of the nanomedicine in vivo was evaluated by bioluminescence imaging monitoring after administration. H&E staining was used to observe the histomorphological changes of organs, and serum biochemical indicators of liver and kidney function were detected.

Results: : The hydrogen and carbon spectra showed that cRGD-Xa was synthesized correctly. TEM showed that the cRGD-Xa NPs were spherical and uniform in size with a diameter of about 34 nm. MTT results showed that the IC50 value of cRGD-Xa-NPs on 4T1 cells was 14.81 μM, which was better than that of Xa (22.66 μM). WB analysis showed increased expression of Bax, c-PARP and c-Caspase-3 and decreased expression of Bcl-2. In vivo biodistribution imaging results showed that cRGD-Xa NPs@ICG could be effectively enriched in tumor tissues. The experimental results of orthotopic breast cancer model showed that cRGD-Xa NPs group could effectively inhibit tumor growth, and serum biochemical indexes and organ H&E sections showed that cRGD-Xa NPs had good biological safety.

Conclusion: In this study, a novel self-assembling nanomedicine cRGD-Xa NPs was successfully constructed and systematically evaluated to overcome the limitations of Xa in targeting and amphiphilicity. The results show good physical and chemical stability and excellent tumor targeting ability in vitro and in vivo, which provides a promising strategy for the design and development of self-assembly nanoformulations of active ingredients of traditional Chinese medicine for tumor specific therapy.

Construction and application of Xanthatin nanoparticles triggered by tumor acidic microenvironment

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Background: Breast cancer is characterized by high metastasis and recurrence rates, which often cause adverse reactions and drug resistance during radiotherapy and chemotherapy. Xanthium Pavilion, as the main active component of Xanthium from Asteraceae, has a clear inhibitory effect on gastric cancer, lung cancer, colon cancer and other tumors. However, there are problems such as poor water solubility and low bioavailability, which will increase the risk of toxicity.

Purpuse: In order to more accurately and effectively play the effect of xanthium pavilion, the present study combined with nanotechnology was used to provide a new targeted therapy for breast cancer.

Method: To design and construct cRGDUXa, a polypeptide nano-preparation of xanthatin (Xa), which is activated by tumor acidic microenvironment, to improve the efficacy of Xa and reduce its toxicity, and to study its effect on 4T1 mouse breast cancer cells.The shape of cRGDUXa nanoparticles was determined by transmission electron microscopy. The size of drug nanoparticles was measured by dynamic light scattering.

MTT assay was used to detect the effect of different concentrations of cRGDUXa on the viability of mouse breast cancer 4T1 cells. The uptake of cRGDUXa to 4T1 cells was observed by laser confocal microscopy. The effect of cRGDUXa and Xa on lysosomal membrane permeability was detected by lysosomal membrane permeability (LMP) kit. Western blot was used to detect the expression of apoptosis pathway proteins after treatment. Finally, the in vivo experiment was carried out by establishing a breast cancer 4T1 cell xenograft tumor model in mice. The tumor growth was monitored after drug administration, and the biological safety was evaluated.

Results: cRGDUXa nanoparticles were spherical and uniform in size. The particle size of the nanoparticles was about 110 nm by dynamic light scattering (DLS). The IC50 of cRGDUXa in 4T1 cells was 12.54 μM, which was better than that of the Xa (17.61 μM). Laser confocal observation showed that cRGDUXa could target the lysosomes of tumor cells and induce enhanced lysosomal membrane permeability (LMP). WB assay detected the pro-apoptotic protein Bax and anti-apoptotic protein Bcl-2, and found that the ratio of Bax/Bcl-2 was increased, and the expression of Cleaved Caspase 3 was increased. It can inhibit the growth of transplanted tumors and has good biosafety in tumor treatment in vivo.

Conclusion: cRGDUXa nanomedicine can significantly inhibit the proliferation and apoptosis of 4T1 cells, and may be used as a potential anti-tumor drug.

Exploring clean & green methods for obtaining astaxanthin from natural resources for pharmaceutical and beyond purposes

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Background: Astaxanthin is a high-value lipophilic carotenoid with recognised antioxidant and promising anticancer properties. It has been sourced naturally from marine organisms, particularly microalgae such as Haematococcus pluvialis, or synthesised chemically from petrochemical precursors. However, synthetic astaxanthin raises concerns as it may carry toxic intermediates. Recently, researchers successfully engineered cyanobacteria to synthesise astaxanthin, representing a potential sustainable source of astaxanthin that may help meet the growing industrial and biomedical demand. Numerous extraction methods have been developed to extract astaxanthin, including conventional organic solvent-based methods. However, these methods generate large volumes of organic waste, posing environmental concerns. In addition, such methods often involve high temperatures and prolonged extraction times, which can compromise carotenoid stability due to their thermolabile and photosensitive nature. Furthermore, the safety and purity of the final product may be affected by residual hazardous solvents which must meet regulatory standards. Therefore, alternative extraction techniques such as supercritical carbon dioxide (scCO2) have emerged as promising alternatives. scCO2 is a green solvent offering high selectivity and efficiency for lipophilic compound extraction while avoiding many drawbacks associated with conventional extraction. scCO2 methods also have some drawbacks, including the high equipment cost, difficult setup process, and technical knowledge of phase behaviour that needs understanding of physical-chemical interactions between solute and solvent, essential for the effectiveness of the extraction.

Objectives: To evaluate the efficiency and effectiveness of scCO2 extraction of astaxanthin from engineered cyanobacteria and assess the biological activity of the resulting extracts.

Method: A screening supercritical fluid extraction study conducted to establish suitable operating conditions using a 100 mL Helix unit. A two-factor full factorial design is applied to evaluate the effects of temperature and pressure on astaxanthin yield and purity in comparison to ethanol extraction as a reference method.
•A high-performance liquid chromatography (HPLC) method developed and validated using limit of detection (LOD), limit of quantification (LOQ), accuracy, precision on inter- and intra-days basis for estimating the amount of astaxanthin in the extracts.
•Preliminary biological activity assessment of the extracts performed to investigate the effects of astaxanthin-rich extracts on cancer cell viability, matrix metalloproteinase (MMP) activity and TLR4-mediated inflammatory signalling, in comparison to pure astaxanthin.

Results: The validated HPLC method demonstrated acceptable sensitivity and reproducibility for astaxanthin quantification. Initial extraction experiments identified a suitable system configuration; operating conditions associated with improved astaxanthin recovery compared with conventional ethanol extraction. Preliminary $scCO_2$ extraction yielded ~ 2.15 mg/g astaxanthin with ~ 5.3% purity. Cells treated with the crude extract (31.25–125 μg/mL) showed a concentration-dependent reduction in viability, whereas pure astaxanthin at equivalent concentrations had minimal effect. This suggests that other bioactive constituents may be present in the extract. Further optimisation and mechanistic investigations are ongoing.

Conclusion: These findings highlight the potential of supercritical CO_2 extraction as a sustainable approach for bioactive astaxanthin from engineered cyanobacteria. Ongoing optimisation and biological evaluation aim to establish a robust extraction protocol and clarify the therapeutic relevance of the extract.

Development and characterization of a novel topical formulation containing enoxolone

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Background: Enoxolone, or 18β-glycyrrhetinic acid, is a great candidate for dermatological treatments because of its strong anti-inflammatory and skin-soothing effects. The main problem when working with this active ingredient is that it hardly dissolves in water. This poor solubility directly limits how much of the drug can actually penetrate the skin. To fix this issue, finding the right combination of solvents is crucial. The goal is to create a topical product that not only dissolves the enoxolone completely but is also safe, physically stable, and pleasant for patients to apply.

Aim: The objective of this study was to evaluate how well enoxolone dissolves in different solvents in order to design and characterize a safe, stable semi-solid topical formulation containing a final enoxolone concentration of 2%.

Method: First, we tested the solubility of enoxolone in four different solvents: butylene glycol, propylene glycol, pentylene glycol, and ethanol. We analyzed these solvents on their own, and then mixed them together in various binary and ternary combinations. To measure exactly how much enoxolone dissolved in each sample, we used High-Performance Liquid Chromatography (HPLC). Once we had this data, we picked the best solvent mixtures. We didn't just look at their solubilizing capacity; we also made sure the chosen solvents were safe for dermal application while still allowing us to reach our target 2% concentration. Next, we prepared several topical formulations using these selected solvent systems. We tested the physical properties of each candidate to see how well they held up. We checked the pH with a calibrated pH meter to ensure skin compatibility, measured viscosity using a viscometer to confirm appropriate spreadability, and determined the density of the preparations. Finally, to predict long-term stability, the formulations went through accelerated aging protocols. This included standard testing at elevated temperatures and specific heating-cooling (freeze-thaw) cycles. The ultimate selection of the optimal formulation will be based on the integration of these physicochemical and stability parameters.

Results: TBD

Conclusion: TBD

Molecular design, chemical synthesis and transport evaluation of creatine prodrug prototypes

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Background: Cerebral creatine transporter deficiency syndrome (CRT-D) is a neurodevelopmental disorder caused by a defect of the creatine transporter (CRT/SLC6A8) gene. Patients with CRT-D exhibit a lack of creatine in the brain. This syndrome develops neurological symptoms during infancy. A brain creatine replenishment therapy starting from the early stage of brain development would be effective for CRT-D. However, a high-dose oral creatine administration failed in the brain creatine supplementation. Creatine plays an important role in maintaining energy in neurons by storing ATP energy. Creatine is transported from the blood into the brain parenchyma via CRT expressed at the blood-brain barrier (BBB) and neurons. In the patients with CRT-D, creatine cannot be supplied to neurons due to the functional defect of CRT. Therefore, CRT-independent delivery of creatine to the brain is a promising strategy for the CRT-D treatment. The purpose of this study is to develop creatine prodrug prototypes which could be transported by the BBB transporter besides creatine transporter such as glucose transporter and amino acid transporters.

Method: As glucose-creatine prodrug (GCrP), serine-creatine prodrug (SCrP) and tyrosine-creatine prodrug (TCrP), conjugates of creatine–glucose, creatine–serine and creatine-tyrosine were designed, respectively. For chemical synthesis of these compounds, sarcosine methyl ester was first guanidinylated, then condensed with a spacer molecule to prepare a key intermediate. Subsequently, it was condensed with protected glucosamine, serine or tyrosine to afford GCrP, SCrP and TCrP, respectively. The BBB transport was analyzed through the uptake by human cerebral miscrovessel endothelial cells (hCMEC/D3). The cells were incubated with the prodrugs in the presence or absence of inhibitors. The blood-to-brain transport was analyzed by in vivo administration in mice. The activities of cellular uptake and in vivo blood-to-brain transport were quantified by liquid chromatography–mass spectrometry.

Results: The molecular structures of GCrP, SCrP and TCrP were determined by mass spectrometry and NMR analysis. The uptakes of GCrP, SCrP and TCrP by hCMEC/D3 cells were significantly decreased by a inhibitor of glucose transporter

(phloretin), L-serine and L-tyrosine respectively. In contrast, creatine had no effect on TCrP uptake. The brain amounts of GCrP SCrP, and TCrP after their intravenous administration in mice were time dependently increased. These results suggest that GCrP, SCrP and TCrP would be recognized by transporters for glucose, serine and tyrosine, respectively, in brain microvascular endothelial cells and transported to the brain.

Conclusion: We have developed three creatine prodrug prototypes which could be delivered to the brain across BBB via the CRT-independent transporters and transported to brain parenchyma.

Valorisation of cow bone waste into pharmaceutical grade calcium phosphate: A sustainable excipient development and environmental management strategy in Nigeria

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Background: Cow bone (CB) is generated as a waste in large quantities in Nigeria from widespread consumption of the animal meat. This bio waste however, remains largely underexplored for pharmaceutical applications despite its richness in calcium phosphate (CP) (≈ 70%), predominantly as hydroxyapatite. CP is biocompatible, with established medicinal values and pharmaceutical functionalities. Therefore, CB waste could be valorised/converted as alternative source of CP in Nigeria.

This study explored the conversion of CB waste into pharmaceutical grade CP and its functionality as a novel excipient in diclofenac potassium (DP) formulations.

Method: CB wastes sourced from a local abattoir in Nigeria, were thoroughly washed, calcined, powdered, and demineralized using phosphoric acid to yield CP. The CP was purified and characterised for flow properties, elemental composition using atomic absorption spectroscopy (AAS), morphology by scanning electron microscopy (SEM), chemical identity by Fourier transform infra-red (FTIR) spectroscopy, and wet chemistry. Safety evaluation was done using Albino Wistar rats, following ethical protocols. The crude CB and derived CP were employed as diluents in uncoated diclofenac potassium tablets prepared by direct compression and wet granulation, respectively, and as carrier in the solid dispersions, using a commercial CP sample as reference. The formulations were assessed for flow properties, mechanical strength, and in vitro drug release. The data obtained were analysed by paired sample t-test and analysis of variance, using Statistical Package for Service Solution (SPSS), version 25 (IBM® SPSS Statistics 25), and results expressed as Mean ± SD, taking differences between means at $p > 0.05$, as statistically significant.

Results: The extracted CP exhibited excellent flow (5.0 ± 1.0 g/s) properties suitable for producing good quality tablets. There were no detectable heavy metals in the sample, and the FTIR spectrum showed peaks of relevant chemical groups that indicated CP. Crystalline conformations were observed from the SEM micrographs. The acute toxicity studies demonstrated safety of the samples at an oral dose of 5000 mg/kg body weight. The CB-derived CP tablets exhibited mechanical properties (hardness: 8.10 ± 2.16 KgF, friability: 0.1%, disintegration time: 16.71 ± 2.78 min) comparable to those of the commercial CP, with no significant differences ($p > 0.05$). Comparable release profiles were obtained from the tablets in the order: extracted CP > Commercial CP > Crude CB. The solid dispersion also showed very good flow and drug release.

Conclusion: The CB-derived CP, demonstrated very good flow, physicochemical, safety, and functional characteristics suitable for use as diluent and carrier in DP tablets and dispersions. The study is part of our strategic efforts at pharmaceutical raw materials development from local sources for local and global healthcare solutions. It provides a promising pathway for converting an abundant environmental nuisance, into an economically valuable, and sustainable resource, with implications for local pharmaceutical manufacturing, management of CB waste. Further research on the subject is recommended for optimization and other possible applications in science that could bridge health gaps.

Quantitative Bioanalytical derivative spectroscopic studies of Zolpidem tartrate Nanospheres and formulation

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Background: Nanotechnology is a revolutionary path for technological development, which concerns the management of drugs at the nanometer scale. Zolpidem tartrate is used for the treatment of insomnia, which is classified under BCS class I drugs. Zolpidem tartrate is chemically known as N, N, 6- trimethyl -2-(4-methyl phenyl)imidazo[2-a]pyridine-3-acetamide hemitartrate. Perusal of literature reveals that Zolpidem tartrate was determined by liquid chromatographic methods in biological fluids. Spectroscopic methods, such as UV-visible and fluorometric, were developed for Zolpidem. In the present study, the authors attempted to formulate Zolpidem tartrate nanospheres and developed three simple spectrophotometric methods using three indicators (bromocresol green, bromophenol blue, and Sudan red–III)

and determined pharmacokinetic properties (Cmax and Tmax) in biological fluids.

Method: Zolpidem nanospheres were formulated by the solvent evaporation method. The formulated nanospheres were investigated by XRD, and it was found to have a 19.91 at 20°C. Particle size, distribution, and zeta potential were measured using a zeta sizer. The particle size of the prepared nanospheres was found to be in the range of 120–330 nm. The average zeta potential and polydispersity index were 35.07 mV and 0.19, respectively. The morphological characteristics were confirmed by SEM analysis. Calibration studies of Zolpidem tartrate nanospheres are performed by three different indicators: Method I: Bromocresol green; Method II: Bromophenol blue; Method III: Sudan Red III. Zolpidem tartrate nanospheres (10 mg) were formulated as tablets, and consent had been taken from the healthy volunteers, and they were asked to take the drug for 5 days. They were already in treatment with the same drug (zolpidem tartrate 5 mg) daily for 6 months. Ethical Committee approval No: KCP/2025/IEC/0005 from the Mookambiga Medical College, Nagercoil, K K District, Tamil Nadu. The whole study was under the supervision of Dr. M. Jabel, psychiatrist and HOD. The blood samples were collected at the intervals of 0, 10, 20, 30, 40, 50, 60, 70, 80, and 90 minutes. The blood samples were collected in heparinized vacutainer tubes, and the mixture was centrifuged at 3000 rpm for about 15 minutes. The supernatant liquid was collected and freeze-thawed at -10. C.

Results: Zolpidem tartrate nanospheres showed absorbance at ƛ max 201 nm using the zero-order spectrum method. The first-order derivative showed λ max at 305 nm (0.91333) and λ min at 280 nm (0.8041). AUC range: 270 - 340 nm. In similar lines, three methods of indicators have been performed. PK studies revealed that C max was 3564 mcg and T max was 50 minutes.

Conclusion: A simple, precise, and accurate UV spectrophotometric method was developed for zolpidem tartrate nanospheres. The formulated nanospheres were validated in accordance with ICH guidelines. Pharmacokinetic properties were established, and the corresponding C max and T max were established for the zolpidem tartrate formulation. The obtained results were reproducible, with no interference from the polymer matrix in the nanosphere formulation.

Ionic liquid-assisted reverse micellar system for transcutaneous allergen-specific immunotherapy

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Background: The skin is an appealing target tissue for allergen-specific immunotherapy (AIT) because of its dense network of antigen-presenting cells (APCs). However, allergen delivery is severely limited by the physiological barrier of the stratum corneum, which prevents achievement of the desired therapeutic efficacy.

Method: For noninvasive AIT, a paintable ionic liquid-assisted reverse micellar system is designed to enhance transcutaneous allergen delivery. Structurally, the allergen ovalbumin (OVA) is encapsulated within sucrose laurate and dispersed in isopropyl myristate (IPM) to form OVA-loaded reverse micelles (OVA-RM); then, biocompatible ionic liquids (IL) composed of choline hydroxide and oleic acid is utilized as the matrix and permeation enhancer for OVA-RM.

Results: The resulting OVA-RM/IL system facilitates the efficient permeation of encapsulated OVA through the skin, thereby significantly increasing the availability and maturation of skin APCs. After being plastered onto skin, OVA-RM-embedded in IL as a patch provides prolonged OVA retention with minimal irritation. Moreover, the IL-assisted OVA-RM increases the quantity of allergen trafficking to draining lymph nodes in a mouse model of OVA-induced airway allergy, thus inducing effective immune tolerance.

Conclusion: The simplicity and potency of paintable OVA-RM/IL system represent a viable and compelling alternative treatment method for IgE-mediated allergies.

Quality evaluation of dermatological creams formulated with salicylic acid and bioactives from shea butter

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Background: The performance of dermaceutical creams is strongly influenced by the physicochemical characteristics of the formulation base as well as the concentration of incorporated active ingredients. Shea butter and white soft paraffin are commonly employed in topical preparations because of their emollient and occlusive properties however,

they differ notably in their stability, texture and spreadability profiles.
In this study, dermatological creams containing salicylic acid and bioactive components derived from shea butter were formulated and their attributes were evaluated to determine the most suitable base and active concentration for optimal performance. The cream formulations with white soft paraffin as base were compared to the ones formulated with shea butter as the base.

Method: Using the fusion method, five formulations were prepared for shea butter and white soft paraffin bases with each containing salicylic acid concentrations of 0%, 0.5%, 1%, 1.5% and 2%. The prepared creams were subjected to comprehensive evaluation of their physicochemical properties including pH, spreadability, viscosity across varying shear rates and globule size. Functional performance was assessed through antioxidant activity, antimicrobial activity and in-vitro drug release studies with results expressed as mean ± standard deviation. Stability testing was carried out using freeze-thaw cycles and short-term storage under controlled ambient conditions (25 ± 2°C and 60 ± 5% relative humidity for two months) during which changes in colour, odour, texture and phase separation were monitored.

Results: All formulations were confirmed to be oil-in-water creams. Preparations based on white soft paraffin demonstrated higher viscosity and superior stability exhibiting minimal phase changes under both thermal stress and ambient storage conditions. In contrast, shea butter-based creams showed better spreadability and greater cosmetic acceptability although slight softening was observed in formulations containing 0% and 2% salicylic acid. Rheological evaluation revealed pseudoplastic flow behaviour for both bases. Formulations containing concentrations of salicylic acid below two percent concentration achieved the most suitable balance between physical stability, drug release and antioxidant activity. Among all samples, the formulation containing 1.5% salicylic acid emerged as the most stable and functionally effective candidate making it suitable for potential scale-up and further clinical evaluation.

Conclusion: The findings indicate shea butter based formulations are best suited for cosmetic dermatological application while white soft paraffin based formulations are ideal for occlusive therapy, barrier repair and sustained topical delivery. Moderate salicylic acid loading improves overall formulation performance, with the concentrations below two percent salicylic acid representing the most promising dermaceutical formulation. These results highlight the critical role of both base selection and active ingredient concentration in the rational design of innovative, stable and effective topical therapeutic products.

Phytochemical standardization and nanoformulation of delonix regia extract for targeted hepatoprotective drug delivery

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Background: Liver diseases represent a major global health concern and contribute significantly to morbidity and mortality worldwide. Drug-induced hepatotoxicity, viral hepatitis, alcohol consumption, and metabolic disorders are among the common causes of liver injury. Although several hepatoprotective agents are available, their therapeutic effectiveness is often limited by poor bioavailability, lack of targeted delivery, and potential adverse effects. Medicinal plants have gained increasing attention as potential sources of safer and effective therapeutic agents due to their diverse phytochemical constituents. Delonix regia (family: Fabaceae), commonly known as the flame tree, has been traditionally used for its anti-inflammatory, antioxidant, and hepatoprotective properties. Phytochemical investigations have reported that the plant contains various bioactive compounds including flavonoids, phenolic compounds, alkaloids, tannins, and saponins, which may protect hepatocytes from oxidative stress-induced damage. However, the therapeutic potential of plant extracts is often limited by poor solubility, instability, and low bioavailability. Nanotechnology-based drug delivery systems have emerged as promising approaches to enhance the stability, bioavailability, and targeted delivery of plant-derived compounds. Therefore, the present study aimed to perform phytochemical standardization of Delonix regia leaf extract and develop a nano-formulation to improve its hepatoprotective activity.

Method: Leaves of Delonix regia were collected, authenticated, shade-dried, and pulverized into coarse powder. The powdered plant material was subjected to Soxhlet extraction using ethanol to obtain the crude extract. Preliminary phytochemical screening was performed to identify major phytoconstituents including flavonoids, phenolic compounds, alkaloids, tannins, and saponins. Physicochemical parameters such as moisture content, total ash value, and extractive value were determined for extract standardization.
A nano-formulation of the extract was prepared using a nanoprecipitation technique in order to enhance the delivery and stability of the bioactive compounds. The prepared nanoparticles were characterized for particle size, zeta potential, entrapment efficiency, and morphological properties using standard analytical techniques. The hepatoprotective activity of the nanoformulated extract was

evaluated using an in vitro hepatocyte model exposed to oxidative stress conditions.

Results: Phytochemical analysis confirmed the presence of flavonoids, phenolic compounds, tannins, and alkaloids in the Delonix regia extract. Standardization parameters were within acceptable limits, confirming the quality of the extract. The developed nano-formulation showed a mean particle size of approximately 165 ± 8 nm with a zeta potential of −28 ± 3 mV, indicating good stability. The entrapment efficiency was 82.6 ± 2.4%, demonstrating effective incorporation of the extract within the nanoparticle system. Morphological evaluation revealed spherical and uniformly distributed nanoparticles. In vitro studies indicated that the nanoformulated extract significantly improved hepatocyte viability (approximately 87%) compared with the crude extract (approximately 65%) under oxidative stress conditions.

Conclusion: The study demonstrates that phytochemical standardization ensures the quality and consistency of Delonix regia extract, while nano-formulation enhances its delivery efficiency and hepatoprotective potential. The developed nanoparticle system improves cellular uptake and provides enhanced protection against oxidative stress-induced hepatocellular injury. Further in vivo studies are recommended to confirm its therapeutic potential for targeted hepatoprotective drug delivery

Scale-up production of shrimp shell extract-loaded nanostructured lipid carriers (NLC) for cutaneous application

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Background: Shrimp shells are a major by-product of the seafood industry and are often discarded as waste, contributing to environmental challenges. These residues are rich in valuable bioactive compounds such as astaxanthin, a potent antioxidant with significant pharmaceutical potential. However, its poor aqueous solubility and photosensitivity limit its direct incorporation into conventional cutaneous formulations. To overcome this limitation, the use of nanostructured lipid carriers (NLC) is promising, as they enhance solubility, protect, and improve stability of the encapsulated molecules. Although the production of NLC is well established at the laboratory scale, limited data are available regarding process scalability while maintaining product quality. Therefore, addressing scale-up challenges is essential for industrial translation of NLC-based formulations.

Purpose: This study aimed to evaluate the effect of increasing batch volume on the physicochemical properties of shrimp shell extract-loaded NLC, evaluating the maximum production scale while maintaining predefined quality criteria. It was hypothesized that increasing the production volume without adjusting process parameters would affect the NLC characteristics, namely particle size (PS), polydispersity index (PDI) and zeta potential (ZP).

Method: Fourteen batches of shrimp shell extract-loaded NLC (20–300 mL) were prepared using the ultrasound technique. Precirol® ATO 5 and shrimp shell extract were used as lipids, while Tween® 80 and sodium deoxycholate served as emulsifiers, and benzalkonium chloride was incorporated as preservative. The lipid and aqueous phases were heated and homogenized to produce an oil-in-water emulsion, which was subsequently sonicated, cooled in ice bath, protected from light exposure, and stored. Afterwards, PS, PDI, and ZP were measured. Acceptance criteria for cutaneous application were PS < 300 nm, PDI < 0.25, and |ZP| ≥ 30 mV.

Results: From 20 to 150 mL, shrimp extract-loaded NLC formulations maintained suitable sizes D90 < 170 nm and Z-Ave increased gradually from 83 nm to 149 nm. PDI remained < 0.25 up to 100 mL, indicating narrow size distribution. At 125–150 mL, PDI slightly increased (~ 0.26), suggesting moderate increase. At volumes > 200 mL, PS and PDI increased markedly, with PDI ranging from 0.317 to 0.359. At 300 mL, D90 reached up to 395 nm and Z-Ave increased to 227 nm, exceeding the predefined acceptance criteria and indicating greater size heterogeneity. All batches showed negative ZP values ranging from –33 to –38 mV, indicating preserved electrostatic stability. Formulations up to 100 mL fully met cutaneous quality requirements. Volumes > 200 mL showed significant deviation, suggesting insufficient energy input under fixed homogenization and sonication parameters.

Conclusion: The ultrasound production of shrimp shell extract-loaded NLC can be successfully scaled from 20 to 100 mL without compromising critical quality attributes. Beyond 150 mL, a progressive loss of size homogeneity was observed, and volumes > 200 mL exceeded predefined acceptance criteria. These findings demonstrate that scale-up cannot rely solely on proportional volume increase and highlight the need for process parameter optimization to ensure industrial feasibility. Future work will focus on implementing the Quality by Design approach to identify critical parameters and establish a design space that ensures product quality during scale-up.

Optimisation and cytotoxicity evaluation of ibuprofen/zolmitriptan-loaded nanostructured lipid carriers for nose-to-brain delivery in migraine management

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Background: Migraine is a common neurological condition characterized by recurrent episodes of severe headache and associated disabling symptoms. Although monotherapy is the main approach used in the treatment of this disorder, it has limitations, as migraine involves multifactorial mechanisms and a single-drug approach is often insufficient to provide adequate relief. Therefore, combination therapy represents a promising strategy to improve symptom control and clinical outcomes. Nonetheless, some drugs present formulation challenges. Nanostructured lipid carriers (NLC) are promising delivery systems that enhance molecular stability, improve bioavailability, and enable targeted delivery of drug combinations. In addition, the use of alternative administration routes, such as the nose-to-brain route, in association with this type of nanocarrier has shown several advantages. This route bypasses the blood-brain barrier and provides a faster therapeutic onset, which is highly relevant for acute migraine management.

The aim of this work was to optimise two NLC formulations, each containing a drug used in the treatment of migraine and of clinical relevance (ibuprofen - IBU and zolmitriptan - ZOL), and to mix them to obtain a combined IBU/ZOL-loaded NLC formulation for nose-to-brain administration.

Method: The Quality by Design (QbD) approach was applied to optimise the IBU-loaded NLC and ZOL-loaded NLC with respect to the Critical Quality Attributes (CQAs) of particle size (PS), polydispersity index (PDI), zeta potential (ZP) and encapsulation efficiency (EE). The PS, PDI and ZP of the IBU-loaded NLC, ZOL-loaded NLC and IBU/ZOL-loaded NLC were evaluated by dynamic light scattering (DLS), while the EE was assessed by spectrophotometry UV/Vis. These parameters were evaluated for up to 3 months of storage (4.0□0.5ºC and 25.0□0.5ºC) to assess the long-term stability of the NLC formulations. The cytotoxicity of the formulations (0-500 µg/mL) was evaluated in differentiated human neuronal SH-SY5Y cells, through the MTT reduction and neutral red (NR) uptake assays, after 24 hours of exposure.

Results: The individual optimised IBU-loaded NLC and ZOL-loaded NLC formulations exhibited PS, PDI, ZP, and EE values that met the established CQAs. The combined IBU/ZOL-loaded NLC formulation also demonstrated PS, PDI and ZP suitable for nose-to-brain delivery, with values of 98.980 ± 0.249 nm, 0.242 ± 0.002 and -15.143 ± 0.844 mV, respectively. After 3 months of storage at 4.0□0.5ºC, these parameters showed only slight variations, indicating good long-term stability of the combined formulation. Biocompatibility studies in SH-SY5Y cells showed that the IBU-loaded NLC, ZOL-loaded NLC and IBU/ZOL-loaded NLC formulations were safe at concentrations up to 100 µg/mL.

Conclusion: The QbD approach proved to be appropriate for the optimisation of both formulations, enabling the selection of formulations that met the predefined quality attributes for subsequent mixing. The IBU/ZOL-loaded NLC demonstrated adequate characterization results, good long-term stability, and acceptable biocompatibility in neuronal cells, supporting its potential as a promising formulation for combination therapy in migraine management. Additional cytotoxicity assays in RPMI 2650 nasal cells are currently being conducted to assess the safety of this strategy for nose-to-brain delivery.

Substandard quality of the antimicrobials sold in the street markets in Haiti

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This pilot study was conducted to analyze the quality of the antimicrobials sold in the street markets in Port-au-Prince, Haiti. Atotal of 258 packs containing antimicrobials were bought in 28 street markets in Port-au-Prince (Haiti). Tablets and contents of capsules included in 196 packs were analyzed using a Raman handheld spectrometer (NanoRAM of BWTEK, Model: BWS456-785) during the first quarter of 2019. Three out of 11 antimicrobials (Amoxicillin, Metronidazole, and Cotrimoxazole) had a high spectral match with an HQI 90 to the respective authentic medicine for more than 95% of their tablets/capsules. For six antimicrobials (Tetracycline, Erythromycin, Cloxacillin, Azithromycin, Clarithromycin, and the combination Amoxicillin + Clavulanic Acid) none of their tablets/capsules showed a sucient spectral match with the authentic medicine. This finding indicates that these products sold in the markets did not contain the labeled drug and/or contained a degraded drug. In addition to the fact that prescription antimicrobials can be purchased in street markets, the present field study found that for most of them (including “Watch” antimicrobials according to the AWaRe classification) were substandard, which contributes to the present antimicrobials resistance epidemic.

Barriers and facilitators to optimal medication transitions of care in Québec: A qualitative study

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Background: Transitions of care (TOC) represent a high-risk period for medication errors and adverse drug events, which are recognised contributors to avoidable hospital readmissions. Population ageing, multimorbidity and polypharmacy further exacerbate these risks, particularly during transitions from hospital to community care. Medication regimens are frequently modified during hospitalisation and inadequate communication between healthcare professionals can lead to unintended discrepancies once the patient returns home. These discrepancies may result in emergency department visits, rehospitalisations or even mortality. In response to the global burden of medication-related harm, the WHO identified TOC, polypharmacy and high-risk situations as key priorities to improve medication safety. Although pharmacist involvement has been associated with reduced medication-related problems and hospital readmissions, several systemic barriers continue to compromise optimal TOC. These include fragmented clinical information, limited access to hospital records for community pharmacists, lack of standardised procedures, and insufficient interprofessional communication. While international literature has documented these challenges, few studies have explored them within the unique organisational context of the Québec healthcare system. This qualitative study therefore aims to identify barriers and facilitators influencing optimal medication transitions of care across the patient care continuum in Québec.

Method: A qualitative study using focus group discussions will be conducted with healthcare professionals involved in medication transitions of care in Québec. Participants will include community pharmacists, hospital pharmacists, general practitioners in ambulatory practice, physicians specialists, medical residents and nurse practitioners. Each focus group will include eight participants to encourage diverse perspectives while allowing sufficient opportunity for discussion. Groups will be organised primarily by profession to minimise perceived hierarchical dynamics and facilitate dialogue. An additional interprofessional focus group will be conducted to explore collaborative perspectives. Discussions will be conducted virtually, recorded and transcribed. Data will be analysed using inductive thematic analysis supported by qualitative analysis software. Two researchers will independently code the transcripts and inter-rater reliability will be assessed using Cohen's kappa coefficient (≥0.80). Codes will subsequently be organised into categories and themes representing barriers and facilitators to optimal TOC. Member checking with participants and triangulation within the research team will be used to enhance the credibility and rigour. A conceptual map illustrating the relationships between identified barriers and facilitators will be developed.

Results: Data collection for this study is currently ongoing. Results will be ready in June 2026. Results are expected to identify systemic, organisational and interprofessional factors influencing medication transitions of care in Québec. Preliminary hypotheses suggest that barriers may include fragmented information systems, limited access to clinical data, workload pressures, time constraints and unclear professional roles. Facilitators are anticipated to include increased pharmacist involvement during hospitalisation and after discharge, improved access to shared electronic health records, structured communication tools, and stronger interprofessional collaboration.

Conclusion: This study will provide an in-depth understanding of the barriers and facilitators influencing medication transitions of care within the Québec healthcare system. By capturing the perspectives of multiple healthcare professionals involved in the patient care continuum, the findings will contribute to the development of contextually adapted interventions aimed at improving medication safety and continuity of care.

Supercritical CO_2 extraction and process-integrated fractionation of leonotis leonurus for enhanced phytochemical selectivity in pharmaceutical applications

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Background: The development of plant-derived therapeutic products requires reproducible, scalable processing approaches that generate chemically consistent, pharmaceutically suitable materials. Conventional solvent extraction often produces heterogeneous extracts with variable compositions, which limits downstream formulation and manufacturing. Process-integrated extraction and fractionation strategies may enable selective phytochemical concentration and improved compositional consistency for pharmaceutical applications.

Purpose: This study evaluated whether supercritical CO_2 extraction combined with process-integrated fractionation could enhance phytochemical selectivity and biological relevance of Leonotis leonurus compared with conventional solvent extraction.

Method: Leaves of Leonotis leonurus were extracted by conventional maceration using methanol, distilled water, and hexane to obtain crude extracts. These were compared with fractions produced by supercritical CO_2 extraction under

controlled temperature and pressure conditions, enabling selective extraction and in-line fraction collection. Phytochemical profiles were evaluated using chromatographic methods, including thin-layer chromatography (TLC), High-performance liquid chromatography (HPLC), and Fourier transform infrared spectroscopy (FTIR). Total phenolic and flavonoid contents were quantified using the Folin-Ciocalteu method and aluminium chloride colourimetric assay respectively, and antioxidant activity was quantified by the DPPH radical scavenging assay. Biological relevance was assessed using an in vitro monoamine oxidase B (MAO-B) inhibition assay.

Results: Supercritical CO_2 extraction with integrated fractionation generated fractions with improved phytochemical enrichment and clearer chemical separation relative to conventional maceration extracts. Chromatographic and spectroscopic analyses demonstrated a more defined distribution of phytochemical constituents across collected fractions. Selected fractions exhibited higher phenolic and flavonoid contents and antioxidant activity. Several fractions also showed increased MAO-B inhibitory activity compared with corresponding extracts from the maceration method, indicating concentration of bioactive constituents following process optimisation.

Conclusion: Supercritical CO_2 extraction, coupled with process-integrated fractionation, enhanced the phytochemical selectivity and bioactivity of Leonotis leonurus preparations. These findings support the application of sustainable pressure-assisted extraction technologies in early-stage pharmaceutical processing of natural product-derived therapeutics.

Topical ionic liquid-mediated GLUT1 gene editing ameliorates psoriasis and prevents recurrence

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Background: Psoriasis is a chronic inflammatory skin disease with high recurrence rates and limited treatment options. GLUT1 is over-expressed in psoriatic lesions, driving inflammation via glycolysis. Although CRISPR-Cas9 enables gene editing, its topical application is hindered by poor skin penetration. This study developed a choline-based ionic liquid (CIL) to deliver Cas9 ribonucleoprotein (RNP) targeting GLUT1 for psoriasis treatment and recurrence prevention.

Method: CIL was synthesized via acid-base reaction and characterized by NMR, FTIR, and DSC. CIL-RNP complexes were assessed for stability, skin penetration, and gene-editing efficiency in vitro and in vivo. Anti-inflammatory effects were evaluated in HaCaT and RAW264.7 cells, and therapeutic efficacy was tested in IMQ-induced psoriasis mouse models, including recurrence models. Safety was assessed by histology, serum biochemistry, and whole-genome sequencing (WGS).

Results: CIL enabled efficient transdermal delivery of RNP, achieving 76.59% GLUT1 editing efficiency in vivo, primarily via large deletions. CIL-RNP suppressed keratinocyte proliferation, reduced inflammatory cytokines (IL-1β, IL-6, CXCL8), and modulated macrophage polarization. In vivo, it alleviated epidermal hyperplasia, reduced immune infiltration, and restored Th17/Treg/TRM balance. No significant toxicity or off-target effects were observed.

Conclusion: The CIL-RNP platform enables safe and effective topical GLUT1 gene editing, alleviating psoriasis and reducing recurrence risk, offering a promising non-viral therapeutic strategy.

Breaking the Blood–Brain Barrier: Intranasal Spanlastic Nanovesicles for Targeted Brain Delivery of Repositioned Rolapitant in Glioblastoma

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Background: Glioblastoma (GBM) remains the most prevalent and lethal primary brain tumour, characterised by aggressive progression, high recurrence rates, and a median survival of approximately 15 months despite multimodal therapy. A major challenge in GBM management is the blood–brain barrier (BBB), which significantly limits the delivery of chemotherapeutic agents to the brain. Drug repositioning offers a time- and cost-efficient strategy to identify new therapeutic indications for approved medicines. Rolapitant (RP), a neurokinin-1 (NK-1) receptor antagonist currently approved for the prevention of chemotherapy-induced nausea and vomiting (CINV), has recently demonstrated potential anticancer activity. This study aimed to develop and evaluate a nanotechnology-based delivery system to enhance the brain targeting and therapeutic performance of RP for GBM treatment.

Method: Spanlastic nanovesicles (SNVs), elastic surfactant-based carriers, were utilised as a nano-delivery platform to improve RP permeation across biological barriers. RP-loaded SNVs were prepared and characterised for particle size, polydispersity index, zeta potential, entrapment efficiency (EE%), stability, and surface morphology. In vitro release studies were conducted to assess drug release kinetics. Cytotoxicity was evaluated using U87-MG human

glioblastoma cells to determine antiproliferative activity. Furthermore, in vivo biodistribution and pharmacokinetic studies were performed following intranasal administration of radiolabelled RP-SNVs to investigate brain targeting efficiency and systemic exposure.

Results: The optimised SNVs demonstrated a particle size below 200 nm, narrow size distribution, and a negative surface charge, indicating good colloidal stability and suitability for brain delivery. High entrapment efficiency (>80%) confirmed efficient drug incorporation. Morphological analysis revealed spherical, well-dispersed vesicles. In vitro release studies showed a sustained release profile extending up to 8 hours compared with free RP. Cytotoxicity studies demonstrated significantly enhanced antiproliferative activity of RP-loaded SNVs against U87-MG cells relative to the free drug. In vivo findings revealed that intranasally administered RP-SNVs achieved superior brain accumulation, enhanced bioavailability, and prolonged residence time in brain tissue, indicating efficient nose-to-brain delivery.

Conclusion: This study demonstrates the successful repositioning of rolapitant using a spanlastic nanovesicle platform for glioblastoma therapy. The developed system enhanced drug delivery across the BBB, improved cytotoxic efficacy, and exhibited favourable pharmacokinetic characteristics. Intranasal administration represents a non-invasive and clinically translatable route for targeted brain delivery. These findings highlight the potential of nanotechnology-enabled drug repositioning as an innovative strategy to address unmet clinical needs in GBM management and support further preclinical and clinical investigation.

Design and optimization of chondroitin-engineered Cd44-targeted nanoliposomes co-delivering repurposed metformin and bioactive thymoquinone in breast cancer management

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Triple-negative breast cancer (TNBC) remains a global health crisis, accounting for significant mortality in females due to its aggressive metastatic behavior and the lack of estrogen, progesterone, and HER2 receptors, which renders traditional hormonal and targeted therapies inefficient. To overcome these challenges and the limitations of conventional chemotherapy, this study aims to develope a novel targeted nanotherapeutic system repurposing the antidiabetic drug Metformin (MTF) in combination with Thymoquinone (TQ), a bioactive compound from Nigella sativa. Chondroitin sulfate (CS)-coated nanoliposomes were employed to specifically target CD44 receptors overexpressed on TNBC cells.

Liposomes were fabricated utilizing ethanol injection method, followed by a two-stage optimization process. In the initial phase, encapsulation efficiency and drug loading were maximized through sequential analysis, identifying sonication time, TQ:MTF ratio, and a stearyl amine molar concentration as the fundamental parameters. Subsequently, a three-factor, three-level Box-Behnken experimental design was employed to optimize the coating process by investigating the effects of CS concentration, stirring time, and incorporation rate on the coated nanoliposomes physicochemical features.

The design yielded a quadratic model that identified an optimal CS concentration of 0.8 mg/mL, resulting in spherical vesicles with a mean particle size of 173.6 ± 3.45 nm, a narrow polydispersity index of 0.120, and a highly negative zeta potential of −54.20 ± 0.32 mV. Structural characterization via transmission electron microscopy confirmed the existence of integral coating layer, while differential scanning calorimetry and Fourier transform infrared spectroscopy analyses verified the successful molecular entrapment of both drugs while maintaining their chemical integrity and compatibility. In vitro release studies in PBS revealed a strategic biphasic profile: the hydrophilic MTF exhibited rapid release following Higuchi kinetics, whereas the lipophilic TQ showed a sustained release profile governed by the Korsmeyer-Peppas model. This differential release kinetics is hypothesized to prime cancer cells with metabolic stress via MTF before the apoptotic action of TQ takes effect. Extensive cytotoxicity evaluations against MDA-MB-231 TNBC cells demonstrated that the optimized CS-coated liposomes restored potent synergism with a Combination Index (CI) of 0.72. The formulation significantly reduced the IC50 values to 20.1 µg/mL for MTF and 6.7 µg/mL for TQ compared to the free drug combination. Furthermore, the optimized formulation maintained high cell viability in human skin fibroblasts, indicating superior selectivity and safety compared to non-targeted treatments.

These findings collectively highlight the potential of Chondroitin-coated dual-drug nanoliposomes as a promising, synergistic, and targeted therapeutic strategy for the effective management of Triple-negative breast cancer.