FIRST POSTER PRIZE

P-II-10

3D-printed lipid mesophases for the treatment of chronic liver disease

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Introduction: Lipid-based formulations offer a promising strategy for improving the oral bioavailability of lipophilic drugs, but their integration into solid oral dosage forms faces challenges due to high viscosity and heat sensitivity. This study employed semi-solid extrusion to produce 3D-printed tablets, or printlets, rich in bioactive lipids [1]. A lipid mesophase (LMP)-based ink of S80, vitamin E, and water, was used for additive manufacturing. In the context of chronic liver disease treatment, the inclusion of S80, a natural phospholipid, is interesting due to the deactivation of profibrogenic hepatic stellate cells [2]. The printlets' efficacy in delivering poorly water-soluble drugs through a self-emulsification process was exemplified by the incorporation of obeticholic acid.
Aims: To develop an LMP-based solid oral dosage form using semisolid extrusion 3D-printing for the treatment of chronic liver disease, capable of enhancing drug solubility and bioavailability through a self-emulsification process.
Methods: The LMP composition was screened to optimize printability, shape retention, and disintegration. The formulation was characterized in terms of drug content and homogeneity, by HPLC, phase identity by SAXS, and rheological properties. The printlets' behavior in the gastrointestinal tract and the self-emulsification mechanism were evaluated via SAXS, Cryo-TEM, and drug release profiling in simulated fluids. *In vitro* tests assessed effects on intestinal barrier integrity and hepatic cell antifibrotic activity.
Results: A ternary system consisting of 68% S80, 20% water, and 12% vitamin E exhibited optimal mechanical properties. Homogeneous drug distribution within the printlet was confirmed. SAXS measurements revealed the coexistence of inverse hexagonal and lamellar phases, crucial for printability and disintegration. Rheological characterization demonstrated that the printing process enhanced the structural strength of the LMP. Printlets remained intact in acidic conditions with no drug release in simulated gastric fluid, but fully disintegrated in simulated intestinal fluid within 6 h. The self-emulsification process was confirmed by the abundance of micelles and vesicles in Cryo-TEM images. This colloidal system did not compromise the viability and permeability of intestinal epithelial cells. Moreover, antifibrotic activity in LX-2 cells was observed, as evidenced by increased expression of the PLIN2 gene and the presence of cytoplasmic lipid droplets.
Conclusions: This study effectively applied lipid mesophases for semi-solid extrusion 3D-printing, showing promise in delivering poorly water-soluble drugs through self-emulsification. With enhanced drug solubility, coupled with co-formulation with hepatoprotectants, the printlets hold potential as an oral treatment for chronic liver disease.

Keywords: Lipid mesophases, 3D-printing, semi-solid extrusion, oral delivery, chronic liver disease.

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SECOND POSTER PRIZE

P-IV-4

Digital healthcare services in community pharmacies: The Pneumoscope™ case study

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Introduction: New healthcare devices based on artificial intelligence are spreading, opening up novel opportunities for innovative-health pharmaceutical services in decentralised primary care settings. The Pneumoscope™, a smart stethoscope, is an innovative digital tool that recognises lung sounds by associating them with specific respiratory pathologies using artificial intelligence. Effective triage and early detection methods implemented in primary health care settings such as community pharmacies (CPs) could help reduce pressure on hospital emergency departments, healthcare systems and save lives.
Aims: To understand how the Pneumoscope™ could be implemented in the healthcare system, this research aims at analysing the pharmacists' and patients' readiness to use this device for respiratory disease screening in CPs in the French speaking part of Switzerland.
Methods: A 2-stage exploratory cross-sectional study was conducted: 1) a qualitative analysis using semi-structured interviews and focus groups to understand the management of patients with respiratory problems and the pharmacists' readiness of using the Pneumoscope™ in their daily clinical practice; 2) a quantitative questionnaire on patients' readiness to use the Pneumoscope™ and on their level of confidence in AI in the healthcare domain. Data collection and analysis was carried out by two Master's students.
Results: Pharmacists see great potential in integrating e-health services into their daily clinical practice to improve their legitimacy in advanced triage and interprofessional collaboration in care coordination with physicians. Most patients were satisfied with the care they received in CPs, and patients readiness of the Pneumoscope™ was correlated with their level of confidence in AI ($p=0.0092$) and with their CP location ($p=0.0276$).
Conclusions: Digital devices such as the Pneumoscope™ enable pharmacists to use their skills and knowledge to enhance their clinical engagement in patient care and public health. Scientific evaluation of the Pneumoscope™'s effectiveness in interprofessional collaboration in primary care and role definition are essential steps towards recognition by health authorities and reimbursement by health insurers.

Keywords: Triage, Pneumoscope™, respiratory symptoms, COVID-19, artificial intelligence, community pharmacist, interprofessional collaboration, primary care

THIRD POSTER PRIZE

P-II-5

Developing a novel solubility measurement technique based on second harmonic generation

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Introduction: Understanding the molecular behaviour and solubility of poorly water-soluble drugs (PWSDs) is crucial as it directly affects their absorption and bioavailability. Traditional solubility measurement methods are time-consuming and require larger amounts of compounds and solvents. We present a novel technique utilizing second harmonic generation (SHG), a nonlinear optical method [1], to measure solvent redistribution around drug molecules, thereby detecting aggregation onset and stable aggregate formation.
Aims: This pilot study aims to: (i) evaluate the efficacy of SHG in determining solubility thresholds of model PWSDs, and (ii) compare SHG results with conventional solubility data.
Methods: Molecular aggregation and solubility of four PWSDs (amiodarone, felodipine, meclizine, miconazole) were measured in phosphate buffer of pH 6.5 at room temperature. Samples, prepared by antisolvent addition method in 96 well-plates, were illuminated with an ultrafast laser (1030 nm, 66.667 kHz, ~250 fs). Optical filters and lenses selectively collected the second harmonic beam (515 nm), which was directed to a photomultiplier tube (PMT). Detection electronics integrated the light collected by the PMT and converted it to voltage. Second harmonic (SH) intensity values were normalized, followed by linear interpolation and baseline calculation. A three sigma (3σ) limit from the baseline determined the solubility threshold.
Results: Solubility was determined for selected PWSDs by assessing the SH intensity as a function of concentration. The values correlated well with literature data. At low concentrations, intensity values remained steady, indicating a linear response (baseline). Near the solubility limit, drug molecules began to form clusters or aggregates, decreasing the system symmetry, resulting in increased SH intensity (deviation from the baseline). For amiodarone, the SH intensity values showed both a clear solubility threshold and a complex pattern at higher concentrations. This pattern suggested transient structural reorganization within the aggregates and a micelle formation, consistent with the amphiphilic structure of amiodarone and its known critical micelle concentration.
Conclusions: This pilot study introduced a novel optical SHG-based technique to measure the solubility of selected drugs. The measured solubilities aligned well with literature values, demonstrating advantages in precision, speed, and reduced resource consumption over traditional methods. Additionally, the technique offered insights into the molecular dynamics of drug molecules in solution phase, though further research is needed to fully explore its potential.

Keywords: Poorly water-soluble drugs, solubility measurement, second harmonic generation, nonlinear optics, molecular aggregation

Reference:

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BEST POSTER IN PHARMACEUTICAL TECHNOLOGY

P-II-4

Proteomics-supported improvement of TFAMoplex-mediated transfection

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Introduction: Current non-viral gene delivery systems, including lipid and polymer-based methods, primarily focus on protection, uptake and endosomal escape for DNA delivery. However, these approaches often encounter challenges with efficient cytoplasmic transport and nuclear entry. Our research aims to address these limitations by developing protein-based transfection systems capable of helping DNA throughout the entire delivery process. We introduced the TFAMoplex, a transfection agent derived from mitochondrial transcription factor A (TFAM), which forms approximately 100 nm DNA nanoparticles [1]. The original TFAMoplex featured a bacterial phospholipase for endosomal escape and vaccinia-related kinase 1 (VRK1) to enhance transfection efficiency. However, the precise role of VRK1 in this process remains unclear.
Aims: This study seeks to characterize and enhance the TFAMoplex by replacing VRK1 with dynein light chain proteins, specifically RP3, to improve cytosolic transport by directly tethering the complexes to the dynein motor complex.
Methods: Various TFAMoplex formulations were prepared and characterized for size, zeta potential, and transfection efficiency. Binding kinetics between TFAM-RP3 and dynein intermediate chains were assessed using a luminescence-based assay. Additionally, a proteomics-based assay was implemented to compare protein interactions among different TFAMoplex variants [2].
Results: Significant differences were observed in the transfection efficiencies of TFAMoplexes incorporating different dynein light chain proteins. RP3 was identified as the most effective candidate, with confirmed binding to dynein intermediate chains through both luminescence and proteomics assays. The proteomics analysis also highlighted differences in protein interactors, particularly nucleolar proteins, between the VRK1-containing TFAMoplex and other variants. Incorporating the nucleolar protein leucine-rich repeat-containing protein 59 (LRRC59) into the RP3-TFAMoplex significantly improved transfection efficiency, achieving performance levels comparable to the VRK1-containing system.
Conclusions: Our study shows that TFAMoplexes can be functionally optimized by incorporating alternative protein domains. Direct binding to dynein proteins enhances transfection rates, and the inclusion of the nucleolar protein LRRC59 further boosts transfection efficiency. Moreover, TFAMoplexes outperform commercial transfection agents, such as Lipofectamine.

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Keywords: Nonviral gene delivery, gene therapy, protein engineering, proteomics

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BEST POSTER IN PHARMACEUTICAL BIOLOGY AND PHYTOPHARMACOLOGY

P-I-3

Insights into the mechanism of action of a withanolide derivative in multiple myeloma

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Introduction: Multiple myeloma arises from the clonal proliferation of plasma cells in the bone marrow. Despite the availability of a wide range of drugs, current multiple myeloma treatments are not sufficient to cure patients who often relapse and develop drug resistance. Natural products can be used as a source of inspiration to find new drugs thanks to their structural diversity. A previous structure-activity relationship study on withanolides, which are naturally occurring steroidal lactones, led to the identification of a compound named C13.
Aim: This work aimed to assess the biological activity and the underlying mechanism of C13.
Methods: The antiproliferative activity was measured using the XTT assay after 72 h treatment. Patient plasma cells were isolated from bone marrow aspirate using a CD138+ marker and cytotoxicity was measured after 24 h treatment by flow cytometry using Draq7. The anti-angiogenic activity was evaluated after 48 h treatment through a 3D angiogenesis *in vitro* model. This model allows endothelial vessels to form in a fibrin gel, stimulated by angiogenic factors produced by an upper fibroblast layer. Drug combinations were tested for 72 h, and the combination index was calculated with the Chou-Talalay method using the CompuSyn software. 3D co-culture spheroids were formed with RPMI 8226, mesenchymal stem cells, and endothelial progenitor cells in a 2:1:1 ratio and treated for 48 h. Proteomic analysis was performed after 12 h treatment of RPMI 8226 cells.
Results: To evaluate the antiproliferative activity of C13 in a heterogenous disease such as multiple myeloma, patients' primary malignant plasma cells were used. After 24 h treatment, C13 at 500 nM displayed a similar activity than in the multiple myeloma cell line RPMI 8226 with a percentage of cell viability of 28% compared to the negative control (100%). To assess C13 activity in a more representative model, 3D co-culture spheroids were used. C13 antiproliferative activity was in the high nM range with an IC_{50} of 342 nM. As anti-cancer drugs are mainly given in combinations, the antiproliferative activity of C13, combined with clinically used drugs, was evaluated. Synergistic effects were observed when combining C13 (25 nM), dexamethasone (8 nM), and selinexor (12.5 nM) in RPMI 8226 cells (CI = 0.34 ± 0.09) with high antiproliferative activity (91.5 ± 3.6%). The impact of C13 on angiogenesis, a major tumor-supporting process in the bone marrow microenvironment, was studied. A decrease in the vessel network of about 30% was observed after treatment with C13 at 160 nM compared to the control. The mechanism behind C13 antitumoral activity was then investigated. Proteomic analysis, confirmed by western blot, showed a dose-dependent increase of p21 and a decrease of the cell cycle regulators cyclin D1, cyclin-dependent kinase 4, and cyclin-dependent kinase 6. C13 activity was evaluated in other hematological cancer cell lines (THP-1, HL-60, Jurkat, Jijoye, and Granta-519). IC_{50} values ranged from 24 to 44 nM which are comparable to results found in RPMI 8226 (IC_{50} values of 22 nM).
Conclusion: Based on the above data, the upstream molecular pathways and targets of C13 against multiple myeloma warrant a detailed investigation.

Keywords: Multiple myeloma, natural product, hit compound, mechanistic studies, micro-environment

BEST POSTER IN CLINICAL PHARMACY

P-IV-6

Personalized adherence interventions with electronic monitoring: A case report on polypharmacy management in epilepsy

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Introduction: Epilepsy treatment is challenging due to the necessity of multiple daily regimens of anti-seizure medications (ASM). To determine adherence, therapeutic drug monitoring (TDM) is standard practice but falls short of the assessment of long-time adherence. Electronic monitoring enables a deeper understanding of adherence behavior and tailored interventions may be implemented. We present the case of a male patient, in his mid 30s, with symptomatic multifocal epilepsy and emotional instability since 1999, who manages his triple ASM treatment with pillboxes. He lives independently in a village and is working part-time in the city. Poor adherence led to an unstable course of disease with repeated severe seizure manifestations. In January 2021, his neurologist asked the Pharmaceutical Care Research Group (PCRG) in Basel, Switzerland, to support the patient with optimizing his ASM intake behavior.
Aims: Developing personalized adherence strategies for polypharmacy in epilepsy.
Methods: Baseline adherence was measured in 2021 with the recording card Time4Med™. The patient was then successively offered various adherence aids with electronic monitoring over several weeks: weekly punch cards (Pharmis®) with Time4Med™, and prefilled blister pouches (Medifilm®) in the electronic dispenser Medido®. Taking and timing adherence, correctly dosed days as well as drug holidays were calculated. An interview with open-ended questions on the usability and satisfaction of the devices was conducted in September 2023.
Results: Adherence with personal pillboxes was unsatisfactory leading to an unstable course of disease with recurrent seizures. The punch cards were too bulky so that the patient often left them at home, leading to 64% taking adherence, 63% timing adherence, 47% correctly dosed days and one drug holiday of five days (6 weeks in January to March 2022). Significant improvements in medication adherence metrics were observed with the transition to the electronic dispenser with 93% taking adherence, 90% timing adherence, 86% correctly dosed days (4 weeks in April to May 2023). No medication holiday was recorded during this period. No epileptic seizures were observed during both observational periods with electronic monitoring. Patient-reported feedback on device usability and satisfaction were in favor of the intervention with the electronic dispenser in promoting consistent medication intake and optimizing treatment outcomes.
Conclusions: The case highlights the complex nature of managing polytherapy in daily-life and the importance of personalized adherence interventions. Moreover, patient preferences were crucial in implementing the successful adherence strategy. Overall, the case underscores the value of interprofessional health care in optimizing treatment outcomes in epilepsy management.

Keywords: Adherence, intervention, electronic monitoring, epilepsy, polypharmacy, pharmaceutical care, interprofessional health care