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40th Technology Days
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Book of abstracts

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FOREWORD

Dear colleagues, guests, and the professional community,
I am pleased and honored to present to you the collection of abstracts for the 40th anniversary of the Technological Days conference. This collection is more than just a summary of scientific contributions. It is evidence of the continuity, scientific maturity, and innovative spirit that shape contemporary pharmaceutical technology. It contains professional abstracts from various areas – from classical pharmaceutical forms to modern carrier systems to technological aspects of medical devices, reflecting not only the current state of knowledge, but also future directions of research and practice.
In the context of the four decades of the conference, this anniversary collection is also a symbolic bridge between generations of scientists, pedagogues, developers, and regulators who participate in fulfilling the common goal: to ensure effective, safe, and affordable drug therapy for every patient.
We would like to thank all authors and co-organizers who contributed to the creation of this publication with their expertise and enthusiasm. I believe that the proceedings will bring you not only new knowledge, but also inspiration and impetus for further professional activity.
Sincerely,

PharmDr. Veronika Šimunková, PhD.
Head of the Department of Galenic Pharmacy
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ORAL PRESENTATION

HISTORY OF TECHNOLOGY DAYS SINCE 1967

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Abstract The first Technology Days were held in 1967 (in Smolenice) and were then organized annually until 1991. In the context of political changes in Czechoslovakia, after 1991, they were organized at 2-year intervals—alternating with the Pharmaceutical Technology conference, which was hosted by the Faculty of Pharmacy in Hradec Králové, Czech Republic. Over the years, in addition to Slovak and Czech guests, the Technology Days have also included experts from Germany, Poland, Hungary, Spain, the Netherlands, France, Austria, England, Switzerland, Bulgaria, Denmark, Belgium, and Italy. The topic of the Technology Days has not only always been the current issue of dosage forms, excipients, technological processes, drug evaluation, biopharmaceutical aspects of drug administration into a living organism, but also the preparation of standards such as a pharmacopoeia or codex. A significant contribution to the professional pharmaceutical community was also the "coordination" of terminology in the field of galenic pharmacy. A turning point in the organization of the conference came during the coronavirus disease 2019 pandemic, when the conference was organized in a hybrid form for the first time—onsite and online. This also enabled us to reach a wider audience. Thanks to cooperation with the Slovak Chamber of Pharmacists and the Slovak Pharmacy Students Association, the number of participants is increasing to include pharmacists from public pharmacies and pharmacy students. The topics of the current 40th Technology Days are Nanoparticulate systems in drug delivery, Quality by design and evaluation of medicines, Pharmaceutical compounding, and Medical technologies.

Keywords *Technology Days, history, conference, pharmaceutics*

LUBRICANT MIXTURES: A SOLUTION FOR TABLETS?

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Abstract Lubricants are critical excipients in tablet manufacturing, reducing friction during tablet ejection and preventing sticking to punches. However, lubricant use can adversely impact tablet properties, including disintegration time and tensile strength. This study investigated the feasibility of using binary lubricant mixtures to optimize lubrication efficiency while minimizing negative impacts on tablet properties. Individual lubricants, magnesium stearate (MgSt), sodium stearyl fumarate (SSF), glyceryl dibehenate, stearic acid, micronized poloxamer 188 (P188), micronized poloxamer 407 (P407), and sodium lauryl sulfate were evaluated for their impact on ejection force and tablet properties at concentrations of 0.5%–2.0%. In model tablets with single lubricants, MgSt consistently produced the lowest ejection forces across all concentrations and was statistically equivalent to the best performing lubricant in all tests. SSF also performed well, exhibiting low ejection forces and favorable tablet properties. By contrast, other lubricants exhibited inconsistent results, poor tablet properties, or handling challenges. Binary MgSt–SSF mixtures in model tablets were subsequently investigated, and they demonstrated promising performance, achieving both low ejection forces and robust tablet characteristics. Finally, sitagliptin, a poorly compressible and sticky active pharmaceutical ingredient (API), was incorporated into the final formulation. While lubrication efficiency remained promising, tablet property failures were observed. MgSt–SSF combinations were a promising strategy to optimizing lubrication. However, future work will focus on further tailoring the mixtures for use with challenging APIs.

Keywords *lubricant, mixtures, magnesium stearate, sodium stearyl fumarate, sitagliptin*

REGULATORY REQUIREMENTS FOR MEDICAL DEVICES PLACED ON THE MARKET IN SLOVAKIA

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Abstract In Slovakia, a medical device (MD) or an *in vitro* diagnostic medical device (IVD MD) may be placed on the market only if it complies with all applicable regulatory requirements. These requirements comprise European Union (EU) Regulations, national Slovak legislation, relevant European guidelines (e.g., Medical Device Coordination Group guidance), and internationally recognized standards such as those issued by the International Organization for Standardization. The primary national legislative instruments are Act No. 362/2011 Coll. on Medicinal Products and Medical Devices and Act No. 56/2018 Coll. on Conformity Assessment of a Product and Making a Certified Product Available on the Market.

At the EU level, MDs are regulated by Regulation (EU) 2017/745 on medical devices (MDR) and IVD MDs are regulated by Regulation (EU) 2017/746 on *in vitro* diagnostic medical devices (IVDR). The implementation of MDR and IVDR required the establishment of transitional provisions to accommodate devices previously certified under the repealed directives—commonly referred to as "legacy devices." These transitional timelines are specified in Regulation (EU) 2023/607.

Before market placement, a device must bear the CE marking, which signifies conformity with applicable EU legislation. For devices classified above Class I, the involvement of a Notified Body is required. A Notified Body is an independent third-party organization designated by the European Commission to assess whether the device fulfills all relevant General Safety and Performance Requirements. This includes evaluation of the technical documentation and auditing of the manufacturer.

In Slovakia, MDs and IVD MDs may only be marketed if they are correctly CE marked, accompanied by a Declaration of Conformity issued by the manufacturer, and provided with Instructions for Use and labeling in the Slovak language. Furthermore, for MDs of Class IIa and higher and IVD MDs of Class B and higher, the involvement of the State Institute for Drug Control (SIDC) is mandatory. Economic operators are required to notify the SIDC within 14 days following the placement of such devices on the Slovak market.

Keywords *medical device, in vitro diagnostic medical device, regulatory requirements, Slovakia*

DESIGN AND OPTIMIZATION OF A DELIVERY SYSTEM FOR EPIGALLOCATECHIN GALLATE FROM *CAMELLIA SINENSIS* L.

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Abstract Epigallocatechin gallate (EGCG), the major catechin in green tea, has demonstrated potent antioxidant and therapeutic properties, yet its clinical application remains restricted. EGCG is chemically unstable and degrades upon exposure to light, oxygen, and variable pH, reducing its biological activity. Its oral bioavailability is low due to poor absorption, extensive metabolism, and short half-life, resulting in minimal systemic levels. The hydrophobic character, limited barrier penetration, and potential off-target effects further complicate formulation development [1]. Recent strategies aim to overcome these barriers. Nanoparticle-based carriers, including lipid and polymeric systems, shield EGCG from degradation and enable controlled release. Encapsulation in liposomes, micelles, and nanoemulsions improves solubility, prolongs circulation, and enhances stability [2]. Nutritional bioenhancers and stabilizing agents have been used to reduce metabolism and increase absorption [3]. Alternative administration routes such as mucoadhesive and transdermal systems bypass first-pass metabolism, while hydrogel-based platforms provide sustained release and improved compliance [4]. These approaches represent a comprehensive framework to maximize EGCG's therapeutic efficacy and support its translation into clinical use.

Keywords *epigallocatechin gallate, bioavailability, nanoparticles, drug delivery, stability*

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INNOVATIONS IN THE PREPARATION OF MEDICINE IN THE HOSPITAL PHARMACY OF THE NATIONAL INSTITUTE OF CARDIOVASCULAR DISEASES

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Abstract In recent years, the drug preparation department of the hospital pharmacy has implemented several innovative procedures, the most significant of which relate to the preparation of solid single-dose oral drugs and parenteral nutrition. The introduction of aseptic preparation was a multi-year project preceded by the establishment of a dedicated laboratory and the development of protocols that enabled not only the preparation of parenteral nutrition but also the compounding of cardioplegic solutions. A key innovation in this laboratory is the use of an automatic compounding system, which significantly enhances accuracy, safety, and efficiency by reducing preparation time.

In the area of non-sterile dosage forms, recent advancements reflect a growing emphasis on individualized therapy as a central driver of process redesign. One such advancement is the standardization of dosages prepared using traditional methods; another is the development of new dosage forms that offer multiple advantages.

In addition to conventional liquid forms, a major innovation is the introduction of gel tablets produced using 3D printing technology. This method stands out for its precision, speed, safety, and particularly for its uniformity, which results from the automation of most preparation steps. While current limitations include issues related to dissolution and stability, the supplier is actively working on improvements, further underscoring the innovative nature of the technology.

These developments highlight that even within routine hospital pharmacy operations, there is ample opportunity to engage in pharmaceutical innovation and contribute to advancing the field.

Keywords *automated compounding system, parenteral nutrition, 3D-printed tablets*

BONE SCAFFOLDS FOR TARGETED DRUG DELIVERY AND ACCELERATED REGENERATION

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Abstract In tissue engineering, therapeutic molecules, scaffolds, and cells are crucial to ensure adequate regeneration and tissue function. To ensure therapeutic molecules exert their intended biological effects in an effective manner, they must be adequately loaded into delivery systems to maintain their therapeutic capacity and be released at the target site at a controlled rate. This precise delivery is essential to preserve molecular stability and maximize therapeutic efficacy, ultimately promoting tissue regeneration and functional recovery. Bone grafts are specialized biomaterials engineered to stimulate bone formation. They must support cellular adhesion, vascular infiltration, and integration within the host tissue. In our work, we have developed bone grafts with customizable drug release profiles and high loading efficiency. These multifunctional platforms incorporate drug reservoirs within polymeric matrices, enabling the successful encapsulation and release of a wide range of bioactive agents, including growth factors, cytokines, alendronate, extracellular matrix modulators, and antibiotics. Our engineered scaffolds exhibit tunable release kinetics, with 50% of the drug payload released between 48 h and 3 months, depending on the reservoir composition and material properties. By fine-tuning these parameters, we can tailor the release profile to achieve specific therapeutic outcomes. All scaffolds demonstrated porosity exceeding 75%, along with excellent mechanical integrity. Furthermore, *in vivo* studies confirmed robust bone regeneration 12 weeks post-implantation. Notably, scaffolds incorporating bone morphogenic protein 2 and an extracellular matrix modulator significantly enhanced bone formation. These results underscore the scaffolds' favorable physicochemical characteristics, controlled drug delivery capabilities, and promising potential for clinical bone regeneration applications.

Keywords *tissue engineering, scaffolds, local drug delivery, bone regeneration*

INNOVATION AND MANAGERIAL ASPECTS FOR HEALTHCARE USING ARTIFICIAL INTELLIGENCE AND ROBOTICS

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Abstract Healthcare organizations are focusing on accelerating the effectiveness and efficiency of their non-manufacturing processes. Nowadays, the usage of advanced technologies is crucial in achieving this purpose. The management of healthcare organizations should organize the processes and implement the technologies to relieve the specialists from redundant or time-consuming activities that improve and speed up the satisfaction of the patients. It is a standard today that the computer systems with information systems and application software are commonly used, but new advanced technologies need new management views and decision-making in all healthcare services. Therefore, management of healthcare organizations should adopt digital transformation in the business change supported by enterprise architecture specialists who can facilitate description of the current and future situation of business transformation. At this point, not only artificial intelligence with its techniques and robotics, but also other advanced technologies like the Internet of Things, 3D printing, Big Data, etc., can support the selection of proper use cases for healthcare. In achieving innovations in healthcare, the management of healthcare organizations should not only focus on the final deployment of artificial intelligence and robotics but also evaluate various factors and influences, including the strategy, financials, organization, and personal views. However, deploying new solutions in healthcare is fraught with challenges that the management has to overcome.

Keywords *management, organization, innovation, artificial intelligence, robotics*

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REGULATIONS MDR 745 AND IVDR 746 IN HEALTHCARE

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Abstract In recent years, we have witnessed enormous progress in medical technologies, which have the potential to radically transform the way healthcare is delivered. The European Union (EU) has revised the legislation governing medical devices and *in vitro* diagnostics to align with the developments in this sector over the past 20 years. The priority was to ensure a solid, transparent, and sustainable regulatory framework while maintaining a high level of safety and supporting innovation.

These technologies contribute to more accurate diagnostics, more effective treatment processes, and overall improved quality of life for patients. Innovation and the ability to bring new or improved medical technologies to the market have led to modernization of standards for medical devices and *in vitro* diagnostic medical devices.

The new Regulation (EU) 2017/745 on medical devices (MDR) and Regulation (EU) 2017/746 on *in vitro* diagnostic medical devices (IVDR) replaced directives 93/42/EEC and 90/385/EEC. Unlike directives, regulations are directly applicable and do not need to be transposed into national law.

The new regulations emphasize the safety of the device throughout its entire lifecycle, especially focusing on reprocessed devices, single-use devices that are refurbished, and devices with no intended medical purpose. A key novelty is the Unique Device Identification (UDI) system. The UDI will become essential for publicly available information about devices and studies (via the EUDAMED=European Database on Medical Devices).

There are also changes in labeling requirements, introduction of new terms such as hospital-use only devices, systems and procedure packs, and traceability of devices within healthcare facilities. The requirements stemming from these regulations are intended to ensure transparency and patient safety.

Healthcare professionals are also involved in fulfilling these requirements, which means changing work habits and procedures. The aim is to enhance patient safety by implementing stricter conformity assessment procedures (to prevent dangerous or noncompliant devices from entering the market) and post-market surveillance.

Keywords *health technologies, transparency, patient safety, supervision*

NANOPARTICLE DRUG DELIVERY SYSTEMS FOR DERMAL ADMINISTRATION OF l-ASCORBIC ACID

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Abstract l-ascorbic acid has several beneficial therapeutic effects on the skin: treatment of wrinkles, hyperpigmentation, protection against oxidative stress, especially ultraviolet radiation, effects on wound healing, and anti-inflammation. l-ascorbic acid is naturally accumulated in the skin at levels much greater than in blood plasma, suggesting a natural protection system provided there is adequate nutrition. The question arises whether these natural levels can be boosted by topical dermal administration and whether boosted levels have added therapeutic value. In fact, l-ascorbic acid alone is probably not useful, but a cocktail of other nutrients and active pharmaceutical ingredients (APIs) may be useful. Conventional formulations are inadequate due to poor permeability of this hydrophilic molecule and poor stability. Suitably designed nanoparticle carriers can solve both the stability and permeability limitations of l-ascorbic acid. The task to produce a successful dermal drug delivery system for l-ascorbic acid is a challenging one and will give useful insights into the design of dermal drug delivery systems for other hydrophilic APIs.

In the last 5–7 years, several studies, mostly based on liposome-like nanoparticles, have been shown to carry l-ascorbic acid across *in vitro* model skin models such as porcine skin using Franz diffusion cell. Furthermore, there is release of l-ascorbic acid into the skin model. Some of these drug delivery systems have shown characteristics that contradict simple theoretical expectations, being larger in size than anticipated and possessing a negative surface charge. Some of these drug delivery systems have contradicted simple theory, being much larger than expected and negatively charged. This review discusses the experimental techniques of permeability studies and tape stripping and presents some research studies based on potential nano dermal drug delivery systems to carry l-ascorbic acid.

Keywords *l-ascorbic acid, topical dermal delivery, nanoparticles, permeation studies, tape stripping*

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ADVANCEMENTS AND PITFALLS OF VINIFERINS, OLIGOMERS OF RESVERATROL CONTAINING A (2,3-DIHYDRO)BENZO[*b*] FURAN PRIVILEGED SCAFFOLD

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Abstract Dihydrodimeric and dimeric viniferins, as the plant secondary metabolites "constructed by nature" on the structural framework of a biologically highly precious resveratrol molecule, contain a privileged bicyclic 2,3-dihydrobenzo[*b*]furan or benzo[*b*]furan scaffold. Therefore, they can interact very effectively *in vitro* and *in vivo* with various biomolecule targets and show notably higher affinity and selectivity for the desired targets than other structures. These naturally occurring stilbenoids, as well as their appropriately modified semi-synthetic and synthetic analogs and derivatives, deserve extraordinary attention because they might offer a broad palette of pharmacological effects. These properties can be prospectively used to improve human health. The objectives of the current research were to *in silico* characterize a set of particular viniferins and several of their biologically promising derivatives considering structural, physicochemical, and pharmacokinetic (PK) properties, including the ability to passively permeate through various biological barriers, for example, stratum corneum, intestinal barrier, or the blood–brain barrier. Experimental estimation and accurate calculation of these characteristics are absolutely essential for the structural optimization or the possible preclinical and clinical evaluation of these compounds. The predictions of the PK features were carried out following relevant computational applets and well-known models successfully utilized in medicinal chemistry. In addition, the drug-like and natural product-like profiles of these molecules were predicted considering the values of an efficient quantitative estimate of a druglikeness, natural product score, and Medicinal Chemistry Evolution-18 parameters.

Keywords *Viniferins, privileged scaffold, structure–activity relationships*

Acknowledgment The study was supported by the Slovak Research and Development Agency under Contract No. APVV-22-0133, and the Grant of the Faculty of Pharmacy, Comenius University Bratislava No. FaF/18/2025.

COMPETENCE-BASED EDUCATION AND ASSESSMENT RESEARCH PROJECT PROPOSAL

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Abstract The growing demand for healthcare professionals, the dynamic era of innovation in healthcare technologies, and the increasing competitiveness of universities and colleges are just a few examples of the ongoing changes in society. Competency-based education is a common educational model for healthcare professionals. Understanding and supporting driving factors behind adoption of this model are the key prerequisites to meet the expected outcomes. The aim of the proposed research project is to assess the level of competencies acquired by future graduates of the master's degree program in "Management and Health Technologies."

This 2-year program is jointly conducted by the Faculty of Pharmacy and the Faculty of Management at Comenius University Bratislava, in close cooperation. This project is based on a qualitative survey conducted to explore the complexity of drivers and challenges associated with acquiring the competencies necessary for successful completion of the program and obtaining an attractive job offer as well. The survey involves students and other stakeholders, such as academics, employers, and partners. It aims to explore the impact of factors such as the simplicity and accessibility of educational regulations, study flexibility, the use of modern educational methods, integration of artificial intelligence into teaching, development of knowledge management through integration with practice, personalized approaches tailored to individual student needs, and other modern educational tools. Emphasis is placed on creative solutions, scientific engagement, and internationalization of teaching. The project proposes an in-depth examination of students, enabling an evaluation of the competencies acquired during their studies at both participating faculties of Comenius University Bratislava.

The research outcomes can bring practical recommendations for improving the curriculum and integrating innovative teaching methods. The results may also support future accreditation processes and foster stronger international collaboration, thereby enhancing the program's attractiveness and relevance for both students and the labor market.

Keywords *competences, education, knowledge management, health technology*

DIABETES TECHNOLOGY IN SPORT AND EXERCISE MANAGEMENT FOR INDIVIDUALS WITH TYPE 1 DIABETES

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Abstract Sport and exercise are fundamental to long-term health in individuals with type 1 diabetes; still, maintaining glycemic stability during training or competition remains a major challenge. Fluctuations in insulin sensitivity, carbohydrate availability, and hormonal responses vary with exercise type, timing, and intensity, requiring precise coordination of therapy and nutrition.

This work summarizes current knowledge on the physiological effects of aerobic, resistance, and high-intensity interval exercise on glucose regulation. Special focus is given to pre- and post-exercise strategies, including carbohydrate supplementation, hydration, and insulin adjustments tailored to individual responses.

A key advancement is the integration of medical technologies into exercise routines. Continuous glucose monitoring and hybrid closed-loop insulin systems allow for real-time glycemic tracking and dynamic insulin delivery, reducing the risk of hypo- or hyperglycemia during sport. These systems are now essential tools not only for safety but also for optimizing performance across different levels of physical activity.

Smartphone-connected applications and wearable sensors further support decision-making by providing real-time data on glucose trends, physical activity, and carbohydrate intake. These platforms enhance user autonomy and allow for personalized adjustments, aligning exercise with metabolic needs.

This evolving, technology-driven approach empowers people with type 1 diabetes to engage in sport and exercise more confidently, promoting both metabolic control and physical performance. Emphasis is placed on the importance of translating scientific knowledge into practical routines using accessible and user-friendly technologies.

With ongoing innovation and individualized application, the role of sport and exercise in diabetes care is shifting from a risky variable to a predictable and manageable therapeutic strategy. This paradigm opens new opportunities for sustainable, evidence-based integration of movement into everyday life for people living with type 1 diabetes.

Keywords *diabetes, physical activity, continuous glucose monitoring, closed-loop systems, automated insulin delivery system*

UNLOCKING THE POTENTIAL OF INDIVIDUALIZED MEDICINE: THE STRATEGIC ROLE OF PHARMACEUTICAL COMPOUNDING IN PUBLIC PHARMACY PRACTICE

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Abstract The practice of pharmaceutical compounding in Slovakian public pharmacies is currently in decline, largely due to systemic disincentives. A primary barrier is the inadequacy of the taxa laborum (preparation fee) rates, which fail to compensate pharmacies for the time and expertise required. Furthermore, a poor supply chain dynamic forces pharmacies to purchase large quantities of raw materials, leading to waste and discouraging low-volume compounding. This paper explores the underlying issues and proposes a strategic framework to revitalize this essential pharmaceutical service.

We posit that empowering pharmacists to proactively collaborate with doctors—including general practitioners and specialists—is crucial. By highlighting the unique capabilities of their compounding services, pharmacists can offer doctors an avenue for more precise, patient-specific therapies. This enhanced communication would not only improve treatment outcomes but also elevate the pharmacy's professional standing as a key healthcare provider.

A critical component of this revitalization is securing favorable reimbursement for compounded medications from health insurance companies. This would provide significant benefits: doctors could prescribe truly personalized treatments, and patients would receive customized, affordable care.

To facilitate this, we propose the creation of a standardized formulary tailored for various medical specialties and the establishment of a cooperative network among pharmacies. Such collaborative efforts would strengthen the professional position of pharmacies and provide a strong foundation for future advocacy. Ultimately, a more integrated and valued role for compounding services would justify lobbying efforts to increase the taxa laborum, making the case for fair compensation more defensible to regulatory bodies. This analysis is grounded in extensive professional experience and dialog with pharmacists, doctors, suppliers, and patients.

Keywords *pharmaceutical compounding, taxa laborum, public pharmacy*

BIOACTIVE SURFACTANTS AS AN EFFECTIVE TOOL IN SYNTHESIS AND FUNCTIONALIZATION OF SILVER AND GOLD NANOPARTICLES

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Abstract The presence of bioactive groups such as amide, ester, or urea groups in the molecular structure of single-chain and gemini surfactants provides these molecules with a new level of surface activity and aggregation properties, which depend on the molecular structure of bioactive groups and their location in surfactant molecule. Biological function of these so-called soft surfactants is controlled by their decomposition into structurally simpler products through the hydrolysis of weak ester bonds, often in biological environment[1]. However, amide and urea groups substantially increase hydrophilicity of compounds through their ability to form intermolecular hydrogen bonds[2]. Nanoparticles composed of a metal core and an organic shell gained significant attention in various fields of science and technology due to their unique physical, chemical, and optical properties at the nanoscale. The most studied nanosystems are represented by silver and gold nanoparticles. Silver nanoparticles are applied in medical devices, pharmaceuticals, and coatings in relation to their strong antimicrobial effect. Gold nanoparticles are highly stable nanosystems with distinguished optical properties and potent biological activity such as anti-inflammatory an anti-neoplastic effect, which favors their use in diagnostics, imaging, drug delivery, and therapy of cancer and inflammatory diseases. The current presentation provides an overview of functionalization of silver and gold nanoparticles by bioactive surfactants and shows the relationship between the molecular structure of surfactants and both the physical properties and biological activity of functionalized silver and gold nanoparticles shows the relationship between surfactant molecular structure and physical parameters and biological activity of functionalized silver and gold nanoparticles[3].

Keywords *gold nanoparticles, gemini surfactants, urea, ester bond*

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CAPILLARY ELECTROPHORESIS INDUCTIVELY COUPLED PLASMA MASS SPECTROMETRY: A RENAISSANCE IN PHARMACEUTICALS AND NANOPARTICLE ANALYSIS

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Abstract Over the past decade, we have witnessed a renaissance of capillary electrophoresis coupled with inductively coupled plasma mass spectrometry (CE–ICP-MS). The sensitive element/isotope-specific ICP-MS detection opened a new window to trace qualitative, quantitative, and chiral analysis of metal-containing species or even advanced characterization of nanoparticles (NPs) and nanoclusters with dimensions of 1–10 nm. Novel methodologies for the ultra-trace determination of oxaliplatin enantiomers, pharmacopeial oxaliplatin impurities, and advanced characterization of NPs and their mixtures employing CE–ICP-MS and Taylor dispersion analysis (TDA) will be presented. The chiral CE–ICP-MS analysis provided a baseline separation (R = 2.0) of oxaliplatin and impurity C enantiomers within 9.5 min. The performance characteristics were as follows: limit of detection 125 attomol per injected sample zone, linear dynamic range 0.1–500 µg/mL, and R^2 0.9999. The second work focused on determining oxaliplatin impurity traces by online sweeping preconcentration micellar electrokinetic chromatography coupled with inductively coupled plasma mass spectrometry (MEKC–ICP-MS). Combining online preconcentration (preconcentration factor higher than 1,700 for each impurity) with a sensitive ICP-MS detection resulted in a limit of detection (LOD) LOD of 227 attomol of Pt in the injected sample zone. The fully validated MEKC–ICP-MS method enables determination of 0.0003% of Pt-derived pharmacopeial impurities. Thus, both CE–ICP-MS–based methods could be used in routine pharmaceutical laboratories for quality control purposes. However, the TDA-ICP-MS method was utilized in the hunt to detect and characterize NPs even in complex media mimicking real-life conditions. TDA-ICP-MS allows for unique characterization of NPs' parameters: chemical composition, isotope ratio, hydrodynamic diameter, estimation of particle number concentration, concentration of free metal ions, and surface charge.

Keywords *ICP-MS, capillary electrophoresis, Taylor dispersion analysis, nanoparticles, oxaliplatin, sweeping*

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EXTEMPORANEOUS PREPARATION FOCUSED ON PEDIATRIC PATIENT

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Abstract Pediatric pharmacotherapy comes with its own set of challenges that are not sufficiently covered by commercially available products. Unlike adults, pediatric patients frequently require individually prepared medicines that consider the age and developmental stage, specific dose according to body surface area, or suitable excipients and dosage forms. Hospital pharmacies can provide these customized medications, and therefore are an integral part of the management of pediatric patients. Pharmaceutical compounding can be divided into sterile and non-sterile depending on the drug's properties and its administration route. Sterile preparations, such as parenteral infusions, injections, or eye drops, are done in a cleanroom environment using aseptic techniques to prevent contamination and risk to patient's safety. For example, this allows the preparation of sterile eye drops in pediatric concentrations that are not available commercially or ophthalmic ointments as substitutes in case of a shortage of mass-produced ones. Pharmacists are also responsible for safety and precision during preparation of parenteral drugs, such as cytotoxic chemotherapy or enzyme replacement therapy. In addition to the preparation itself, it includes calculating the correct dose, selecting compatible diluents and materials, and ensuring the sterility and stability of the product is preserved. Non-sterile compounding is used for medications administered orally or topically, such as capsules, ointments, creams, or suppositories. With pediatric patients, complications often arise with them being unable or unwilling to swallow solid oral dosage forms or requiring modified doses. By customizing medications, for instance, creating liquid suspensions, pharmacists can better address specific needs of individual patients.

Keywords *compounding pharmacy, pediatric pharmacotherapy*

QUALITY BY DESIGN APPROACH IN THE DISCOVERY AND DEVELOPMENT OF INDONESIAN BIOACTIVE NATURAL PRODUCTS

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Abstract The quality by design (QbD) approach has been widely used across pharmaceutical research and development. The QbD tools and studies enable the design-based knowledge, risk assessment, mechanistic models, experimental design and analysis, as well as process analytical technology. Indonesian natural products have been reported as sources of bioactive compounds with diverse biological activities. However, it is challenging to implement the QbD approach for the discovery and development of bioactive natural products due to the complexity of chemical and biological properties in medicinal plants. This review aims to discuss various applications of QbD approach related to bioactive compound analysis, identification, determination, and formulation. The combination of experiment design and response surface methodology was commonly applied in the standardization and optimization process to evaluate the content of bioactive compounds, the extraction process, formulation composition, analytical method validation, and instrumentation settings. In addition, despite all the existing challenges, the implementation of QbD approach enables the design-based discovery and development, especially for Indonesian bioactive natural products.

Keywords *bioactive compounds, Indonesia, natural products, quality by design*

SLOVAK PHARMACEUTICAL CODEX

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Abstract Pharmacopeia is a generally binding regulation for the evaluation of the quality, efficacy, and safety of medicines. In 1995, Slovak Republic signed *the Convention on the Elaboration of European Pharmacopoeia* and became a full member of the European Pharmacopoeia Commission. The Contracting Parties have taken measures to ensure that articles of the European Pharmacopoeia (Ph. Eur.) become valid standards used in their own territories.

Ph. Eur. did not contain monographs of stock preparations; therefore, the Slovak Pharmaceutical Codex (SFK) is being published to ensure the quality of medicinal products prepared in pharmacies (individually and mass-prepared medicinal products). The first edition of SFK as national standard was published in 2006, with the supplement published in 2007. SFK, second edition (currently in force), published by Decree of the Ministry of Health of the Slovak Republic in 2015, has two annexes.

According to Act No. 362/2011 Coll. on medicinal products and medical devices, in Slovakia, Ph. Eur. is valid in its original form in English. This situation has created the need to revise SFK as a national standard and make the requirements of Ph. Eur. available for professionals in facilities providing pharmacy care and to other professionals.

The State Institute for Drug Control (SIDC), the Pharmacopoeia Department, in cooperation with the Slovak Pharmacopoeia Commission have prepared the third edition of SFK. It is supplemented by a new General Part, which includes general provisions, reagents, and selected translations of articles from Ph. Eur. To maintain continuity with Ph. Eur., the numbering of methods in SFK is the same as in Ph. Eur. and translated articles refer to their number in Ph. Eur.

Keywords *European Pharmacopoeia, Slovak Pharmaceutical Codex*

DIGITAL INSTRUMENTS FOR ENHANCING PHARMACEUTICAL CARE AND MEDICATION ADHERENCE

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Abstract The primary aim of this pilot study was to explore the feasibility of using a home-based digital tool to track medication adherence and quality of sleep in patients with essential hypertension. Specific goals included comparing medication adherence reported via a validated self-reported questionnaire and an objective digital instrument. The study also aimed to develop a cross-platform mobile app for real-time monitoring of medication intake and sleep quality to analyze adherence patterns and their link to sleep quality.
Long-term management of chronic diseases, such as cardiovascular conditions, is often challenged by poor treatment adherence. Digital instruments have the potential to improve medication adherence and enable more accurate monitoring of the treatment. Evaluation of medication adherence can positively influence healthcare outcomes and reduce public healthcare costs.
A prospective observational cohort study was conducted among patients with essential hypertension. Participants were recruited in person at a community pharmacy and at the Active Aging Centre, Comenius University in Bratislava. After providing informed consent, they completed the validated Slovak version of the 15-STARS questionnaire. Eligible patients then completed an online enrolment form. For 30 consecutive days, participants used a mobile app linked to the REDCap platform to track (1) medication intake logs via a button press and (2) sleep quality, rated daily on a 5-point scale.
Participants classified as nonadherent based on 15-STARS responses showed increased variability in dosing time. Adherent participants took their medication more consistently and reported better sleep quality. Age and gender emerged as potential confounders, highlighting the need for adjustment in future studies.
Limitations include a small, monocentric sample, diagnosis-specific focus, reliance on self-reported data, and the requirements for digital skills.
The study supports the feasibility of comparing medication adherence reported via 15-STARS with our developed digital instrument, while providing insight into users' self-reported sleep quality.

Keywords *medication adherence, hypertension, telemedicine, mobile applications, sleep*

MONITORING OF STORAGE CONDITIONS IN COMMUNITY PHARMACIES AS PART OF GOOD PHARMACY PRACTICE

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Abstract Monitoring of environmental parameters, especially storage temperature in community pharmacies, is undergoing a significant technological transformation. Traditional manual records are increasingly being replaced by automated systems that include continuous recording, alarm functions, and remote access. In this context, the question arises as to whether such a level of technological burden is appropriate, given the actual risks to the stability of medicines under standard community pharmacy conditions. This contribution critically evaluates the proportionality of such monitoring with respect to the principle of "fit for purpose."

The discussion is informed by recommendations from relevant international authorities in the field of good pharmacy and distribution practices, as well as scientific publications on the stability of commonly dispensed dosage forms, including products with increased temperature sensitivity. Sources were selected through a focused literature review targeting regulatory guidelines, pharmacopeial standards, and scientific studies published in the literature. Particular attention was given to data illustrating the practical consequences of temperature excursions in real-world pharmacy settings.

It appears justified to reconsider the scope and nature of environmental monitoring in the pharmacy setting. Applying the principle of "fit for purpose" allows the level of control to be adapted to the characteristics of the stored products. In line with the philosophy of good pharmacy practice, the focus should be primarily on ensuring the quality and safety of medicines for the patient, rather than on the universal application of technical standards regardless of context. Such an approach promotes efficient resource use while maintaining a high standard of pharmaceutical care.

Keywords *monitoring of storage conditions, medicine stability, good pharmacy practice, community pharmacy, fit for purpose*

QUALITY CONTROL OF IBUPROFEN-CONTAINING MEDICINES USED IN PEDIATRIC PRACTICE

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Abstract The thesis focuses on the development of a method for determining the ibuprofen content in suppositories for children, which are prepared in pharmacies during periods of shortage of mass-produced drugs, most commonly oral suspensions. The suppositories were prepared in a pharmacy according to a prescription containing 60.0 mg of ibuprofen per suppository. The ibuprofen content in the commercially available oral suspension was 20 mg/mL. Simple analytical methods – ultraviolet (UV) absorption spectrophotometry and volumetric analysis – were used to determine the ibuprofen content in both dosage forms, without prior separation of ibuprofen from the excipients. A 0.1 mol/l sodium hydroxide solution, a *Titrette* automated burette, and phenolphthalein as an indicator were used for the titration of ibuprofen in suppositories. The suppository was dissolved in a methanol:chloroform mixture (1:1 V/V), and the same procedure was followed for analysis of the oral suspension. For the determination of ibuprofen by absorption spectrophotometry, both standard and sample solutions were prepared in methanol and in the methanol:chloroform mixture (1:1 V/V). Their spectra were measured using a SHIMADZU UV 1800 spectrophotometer in the range of 200–400 nm. Based on the absorbance of the standard solutions recorded at the absorption maxima, the specific absorbance was calculated, and the ibuprofen content in the samples was determined accordingly. Parameters such as repeatability, linearity, and recovery were also evaluated. The results were statistically processed and compared. The ibuprofen content determined volumetrically in the suppositories was 61.50 ± 0.98 mg, and in the oral suspension, 99.12% ± 1.01% of the manufacturer's declared content. When ibuprofen was determined by UV spectrophotometry, the recovery in the standard solutions was 100.92%. The ibuprofen content determined in the suppositories was 62.50 ± 0.01 mg. In the case of the oral suspension, reproducible results could not be obtained due to the negative influence of excipients on the analysis.

Keywords *ibuprofen, suppositories, oral suspensions, UV spectrophotometry, volumetric analysis*

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MODERN METHODS OF USING NANOPARTICLES IN HUMAN MEDICINE

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Abstract Nanoparticles represent a breakthrough sophisticated technology in human medicine, especially in the field of targeted drug delivery, diagnostics, and regenerative medicine. Their small size facilitates efficient systemic circulation and penetration into cellular and subcellular compartments. Because of their unique physicochemical properties – such as high surface to volume ratio, high surface modifiability, and improved ability to cross biological barriers – they enable precise and effective therapeutic targeting with minimal side effects on non-target tissues. The main types of nanoparticles used in medicine include liposome and lipid nanoparticles, polymer nanoparticles, metal nanoparticles (e.g., gold, silver), quantum dots and magnetic nanoparticles based on iron oxides, carbon nanoparticles, hybrid nanoparticles (combination of polymers and metal), mesoporous silicone, and titanium dioxide nanoparticles. Each type has certain specific advantages – from biocompatibility and biodegradability to unique optical or magnetic properties, which are used, for example, in diagnostic imaging techniques. Nanoparticles also represent modern forms in theranostics, where a combination of diagnostic imaging capabilities with therapeutic functions is used, which allows, for example, visualization of tumors and targeting at the same time. Multifunctional nanoparticles have the ability to combine contrast agents, drugs, and ligands providing targeting into a single platform, which facilitates real-time monitoring of treatment responses and, at the same time, personalized advice for therapy. Nanoparticles are already currently used in several areas: imaging methods, diagnostics, regenerative medicine, neurology, cardiovascular diseases, ophthalmology, immunology, antiviral, antifungal, and antibacterial therapy, overcoming drug resistance. Despite significant progress in research and preclinical applications, the efficient, reproducible, and economically viable production of nanoparticles with emphasis on their stability, sterility, and scalability remains a challenge. Another problematic area may be characterization of the interactions of nanoparticles with the biological environment and their long-term impact on the human body, including immunotoxicity and biodistribution. With continued interdisciplinary research, nanoparticles have the potential to fundamentally change the paradigm of modern healthcare in the future.

Keywords *nanoparticles, human medicine, drug carriers, personalized therapy, theranostics*

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TRAINING OF AI SUPERAGENTS BY HEALTHCARE WORKERS

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Abstract We find ourselves at a watershed moment in history: the market value of raw intelligence is plummeting even as its strategic importance in healthcare rises precipitously. Because modern artificial intelligence (AI) systems can now comprehend and execute instructions in natural human language, any practicing clinician – even one with no programming background – can engage in dialog with and progressively refine an intelligent super-AI-agent. This paper examines how such clinician-trained agents can be deployed securely behind hospital firewalls and explores the emerging, indispensable symbiosis between AI agents and healthcare professionals.

Using qualitative workflow mapping in university teaching hospitals combined with rapid prototyping of large multimodal AI models tuned to local clinical guidelines, we propose an iterative coaching framework. In this model, pharmacists, nurses, and physicians interact with the system in everyday language to train specialized sub-agents or full-fledged super-AI agents. We illustrate prototypes capable of reviewing and reconciling medication histories, drafting discharge summaries, and recommending dose adjustments for complex cases of renal insufficiency, while preserving clear human oversight and accountability.

Our findings open three avenues for discussion. First, if machines can absorb practitioners' tacit know-how through conversation and process observation, the mission of health professional schools may shift from simply transmitting expert content to nurturing "meta-expertise": the critical appraisal of machine reasoning, stewardship of patient context, and governance of ethical AI use. Second, therapeutic workflows are bending toward continuous, just-in-time decision support, thereby narrowing the gap between drug discovery and bedside care. Third, accelerated development pipelines that integrate generative chemistry with small-scale virtual trials are redefining pharmaceutical innovation.

Empowering healthcare workers to train AI superagents does not undermine their professional relevance; on the contrary, it will help preserve and even enhance it. Rather than displacing human judgment, these tools will catalyze a new ecology of human–machine expertise in which compassionate, context-sensitive decision-making remains irreplaceable.

Keywords *artificial intelligence, AI superagent, medical education, pharmacy, drug development*

APPLICATIONS OF ARTIFICIAL INTELLIGENCE IN RESPIRATORY DISEASES

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Abstract The increasing complexity and incidence of respiratory diseases present ongoing challenges in clinical practice, particularly regarding diagnostic accuracy and the delivery of individualized patient care. Overlapping symptoms among prevalent airway disorders and subtle changes in disease progression frequently lead to delayed or inaccurate diagnosis, limiting the effectiveness of therapeutic interventions. This project was undertaken to explore whether recent developments in computational technologies, especially artificial intelligence and machine learning, could address current limitations in the detection and management of respiratory conditions.

To approach this question, the investigation focused on recent practical applications of artificial intelligence and machine learning within respiratory medicine. Emphasis was placed on methodologies where computational models draw upon a range of clinical data, imaging results, physiological monitoring, and digital health records. The analysis considered how these models might enhance traditional clinician-led strategies for disease classification, risk estimation, and ongoing assessment of patient status.

Results demonstrate that systems based on artificial intelligence can discern subtle differences between respiratory diseases with similar clinical presentations and reliably identify subgroups of patients who may be at higher risk for deterioration or acute events. Techniques relying on deep learning have achieved levels of accuracy in interpreting imaging studies that closely resemble assessments by experienced physicians. The incorporation of artificial intelligence into digital health devices further allows real-time observation of therapy adherence and symptom progression, which supports earlier and more person-centered clinical interventions.

Despite encouraging outcomes, widespread adoption of these technologies is limited by challenges such as ensuring high-quality datasets, clarity in decision-making processes, and adherence to stringent ethical guidelines for patient data.

In conclusion, artificial intelligence and machine learning offer considerable potential to reshape respiratory medicine, but their ultimate impact will rely on ongoing validation, increased transparency, and strong collaboration across clinical and technical domains.

Keywords *artificial intelligence, machine learning, asthma, diagnosis*

CHITOSAN-BASED FILM-FORMING SYSTEMS WITH CANNABIDIOL

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Abstract Local drug delivery through innovative application forms, such as film-forming systems, enables targeted and sustained delivery of the drug to the site of therapeutic action. Film-forming systems overcome some of the drawbacks of conventional semisolid topical preparations, namely their easy wipe-off from the application site and non-uniform dosing. This study presents the formulation and comprehensive characterization of a novel chitosan-based film-forming system incorporating cannabidiol for antimicrobial topical treatment. First, the highest ethanol–water ratio that allowed optimal chitosan solubilization while minimizing drying time was determined. To maintain an acidic pH, lactic acid was chosen over the commonly used acetic acid due to its superior biocompatibility and its plasticizing effect on chitosan. A suitable cannabidiol solubilizer was identified to ensure its uniform incorporation into the polymer matrix, as well as enhance the skin penetration. The resulting films were characterized using optical microscopy, scanning electron microscopy, Raman spectroscopy, rheological analysis, bioadhesive testing, and differential scanning calorimetry. *In vitro* drug release and permeation studies were conducted on the most promising film-forming system (FFS) FFS formulations. The results demonstrated a homogeneous drug distribution, confirming the solubilizing effect of propylene glycol and the optimal polymer system-to-ethanol ratio. The film-forming systems exhibited excellent bioadhesive properties upon application, with no tackiness observed in the *in situ* formed film after 5 min. Approximately 25% of the active substance was released within the first 8 h, followed by a sustained release over 72 h, which best fits the Higuchi model. Cannabidiol permeation through the Strat-M® membrane was linear over the first 24 h, followed by a plateau phase extending to 72 h, characteristic of sustained-release formulations. The total amount of cannabidiol permeated was 15.94% ± 2.61% of the applied dose. These findings underscore the potential of cannabidiol-loaded chitosan films as a multifunctional platform for the localized treatment of skin infections.

Keywords *cannabidiol, chitosan, film-forming system, topical drug delivery*

BIOSYNTHESIS OF SILVER NANOPARTICLES USING MEDICINAL PLANTS

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Abstract Nanoparticles, with at least one dimension ranging from 1 to 100 nm, are produced by various physical, chemical, and biological processes. Biosynthesis, also known as green synthesis, is a method of producing nanoparticles using natural materials such as plants, fungi, microorganisms, animals, or their products. We synthesized silver nanoparticles (Ag NPs) from the plant extracts of *Origanum vulgare* L., *Lavandula angustifolia* Mill., *Sambucus nigra* L., *Thymus vulgaris* L., *Thymus serpyllum* L., *Berberis vulgaris* L., *Agrimonia eupatoria* L., and others. Aqueous plant extracts with higher concentrations of polyphenols and significant antioxidant activity synthesize Ag NPs faster. The biomechanochemical method combines biosynthesis with mechanochemical grinding, which means that the precursor of Ag NPs ($AgNO_3$) and biological material (plants, eggshell membrane, and various types of lichens) are placed together in a mechanochemical mill. Therefore, it is also possible to use material that has reducing metabolites that are insoluble or poorly soluble in water. Ag NPs exhibit antibacterial effects against Gram-negative and Gram-positive bacteria. A vascular irritability test showed the non-irritating effect of Ag NPs, making them suitable for application to mucosa. We incorporated Ag NPs into thermosensitive *in situ* gels intended for topical therapy in the oral cavity. After application, they change their state from liquid to solid, creating a protective film on the mucosa and prolonging the duration of action and release of nanoparticles and medicinal components of plant extracts. Biosynthetically and biomechanochemically prepared Ag NPs have significant potential for use not only in the prevention but also in the treatment of bacterial infections.

Keywords *nanoparticles, biosynthesis, biomechanochemical synthesis, silver*

DEVELOPMENT OF SUITABLE DRUG DOSAGE FORM FOR ORAL ADMINISTRATION OF CHONDROITIN SULFATE AND FUCOIDAN

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Abstract The aim of this study was to evaluate non-emulsion type oleogels formulated with sorbitan tristearate (STS) and soy lecithin (SL), designed to create an oleogel suspension of chondroitin sulfate (CS) and fucoidan (F) intended for oral immunotherapy. The rheological properties of SL- and STS-based gels in olive oil were determined using a rotational rheometer equipped with cylindrical plate geometry. Measurements were performed at 15°C, 20°C, and 25°C. The stability of the oleogel suspension was assessed by a centrifugation stress test. Texture analysis was conducted using a TAXT Plus Texture Analyzer. Triplicate measurements were analyzed with Exponent software (Stable Micro Systems, Godalming, UK), and results were expressed as mean ± standard deviation. Differences between groups were evaluated by Student's *t*-test. Force–time curves were analyzed, and the calculated parameters were interpreted as hardness, adhesiveness, cohesiveness, and compressibility according to Kulawik-Pióro. The study identified the optimal concentrations of gelling agents required to achieve gel immobility. A stable oleogel environment was obtained with 3% SL (w/w) and 3% STS (w/w) in olive oil. The oleogel exhibited viscoelastic and thixotropic properties influenced by the concentration of gelling agents, temperature, and mechanical stress. The formulated CS–F oleogel suspension demonstrated stability without phase separation at 15°C, while liquefaction occurred above 20°C. The findings indicate that the concentration of gelling agents significantly affects the rheological behavior and transition temperatures of the oleogel structure. An optimal oleogel composition for CS and F encapsulation was identified, suitable for immunotherapy applications, exhibiting a gel state at 15°C that ensures enhanced stability, and transitioning to a liquid state at 20°C, thereby improving the bioavailability of the active compounds.

Keywords *bioavailability, chondroitin sulfate, fucoidan, oleogel, rheology, sorbitan tristearate, soy lecithin, texture analysis*

Acknowledgment *This work was supported by funding from the Slovak Scientific Grant Agency (VEGA 1/0146/23).*

POSTER PRESENTATION

DYNAMICS INTERACTIONS PROFILING OF SERPENTINE AS AN ACETYLCHOLINESTERASE INHIBITOR: AROMATIC INTERACTION OCCUPANCY AND MM-PBSA EVALUATION

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Abstract Bioactive natural products have emerged as potential alternatives for Alzheimer's disease (AD) therapies. Serpentine, an indole alkaloid from *Catharanthus roseus*, has shown stronger acetylcholinesterase (AChE) inhibitory activity than physostigmine in an *in vitro* study. However, its molecular mechanism of inhibition remains unexplored. This study aimed to investigate the dynamic interactions of serpentine in the AChE active site through molecular dynamics (MD) simulations and to estimate the binding free energy through Molecular Mechanics Poisson–Boltzmann Surface Area (MM-PBSA) and energy decomposition analysis. A total of 100 redocking simulations were performed to validate the docking protocol, followed by 100 docking simulations to predict and cluster the best-docked poses. The highest binding energy of the best-docked complex was subjected to 50-ns MD simulations to observe conformational AChE stability and ligand movement in the active site. Binding free energy and key residue contributions were then evaluated using MM-PBSA. The results showed that serpentine formed stable interactions within the AChE active site, with a docking score ranging from 10.404 to 10.543 kcal/mol. Root Mean Square Deviation (RMSD) ligand movement ranged between 0.676 to 2.205 Å during the 50-ns MD simulations, indicating stable binding in the active site. MM-PBSA analysis revealed a binding free energy of −33.102 ± 2.46 kcal/mol during the simulations. Aromatic face-to-face interactions were predominantly observed with Trp84 (99.60%), Phe330 (82.24%), and Trp432 (63.27%), while aromatic edge-to-face interactions involved Tyr442 (51.69%), Tyr334 (90.22%), Tyr121 (38.32%), Trp432 (43.31%), and Phe330 (37.52%). Notably, strong and frequent hydrogen bonds with Asp72 (98.80%) were identified as a major energetic contributor. These findings highlight the pivotal role of the aromatic rings of serpentine in stabilizing the interactions in the AChE active site and provide molecular insights supporting its potential as an AChE inhibitor for AD therapies.

Keywords *serpentine, acetylcholinesterase, molecular dynamics, MM-PBSA, aromatic interactions*

STRUCTURAL CHANGES IN LIPOSOMES INDUCED BY ANTIVIRALS

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Abstract Liposomes are largely used as drug delivery vectors because of their biocompatibility and biodegradability. Due to their dual nature, they can incorporate hydrophilic and hydrophobic drugs. However, the incorporation of a drug into lipid bilayers affects their properties (thermal, structural, surface charge, size, polydispersity, etc.). The present study demonstrates the effect of selected antivirals on the thermal characteristics of phospholipids (gel-to-fluid phase transition temperature, Tm). Two antivirals were selected for the study: favipiravir (FVP) and boceprevir (BCP). Differential scanning calorimetry (DSC) was used to examine their thermal characteristics. The gel-to-fluid phase transition represents changes in the packing of the lipid acyl chains from ordered (gel-like) to highly disordered (fluid-like).

FVP is an RNA-dependent RNA polymerase inhibitor used against influenza viruses (Japan), which was tested in coronavirus disease 2019 (COVID-19) treatments. It is a small, water-soluble molecule. Fully hydrated 1,2-ditetradecanoyl-*sn*-glycero-3-phosphocholine (DMPC) shows Tm at ~24°C. DSC thermograms of DMPC with a different amount of FVP were not affected by the drug up to 0.5 FVP/DMPC molar ratio. Thus, FVP does not incorporate into the hydrophobic region of the lipid bilayer. However, BCP is a lipophilic protease inhibitor that was previously used to treat hepatitis C and was also tested during COVID-19. The phase transition temperature Tm of DMPC was significantly changed. Perturbation of the ordered structure of DMPC acyl chains resulted in a drop in Tm. 1-Palmitoyl-2-oleoylphosphatidylethanolamine (POPE) has one double bond per lipid molecule, and fully hydrated POPE has Tm ca. 26–27°C. The phase transition temperature of POPE was only slightly changed by BCP to a 0.5 BCP/POPE molar ratio. We hypothesize that the less tight acyl chain packing of POPE compared to that of DMPC allows easier accommodation of the antiviral in the bilayer.

Keywords *liposomes, antiviral, drug delivery, DSC*

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QUALITY CONTROL OF THERAPEUTIC PEPTIDES BY CAPILLARY ZONE ELECTROPHORESIS WITH REPEATED SAMPLE INJECTION STRATEGY

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Abstract Biologics are modern therapeutic modalities which are gaining importance in the therapy of serious diseases. Therapeutic peptides represent a bridge between small molecular drugs and biologics. Therapeutic peptides together with biologics are categorized as biopharmaceuticals. The development and production of biopharmaceuticals is accompanied by increased demands on their quality control. Therefore, it is necessary to dispose with accurate and reliable analytical approaches. The analytical methods based on liquid chromatography are the convenient approaches used in the quality control of therapeutic peptides. However, capillary electrophoresis (CE) is emerging as a promising green alternative. CE performed in hydrodynamically closed system offers to obtain concentration sensitivity close to that of a modern ultra-high-performance liquid chromatography. Here, a new CE-UV approach with repeated sample injection (RSI) strategy has been developed for determination of two therapeutic peptides – triptorelin and lanreotide. The separation was carried in the background electrolyte composed of 50 mM formic acid. RSI was realized under a time interval of 100 s for triptorelin and 80 s for lanreotide. The validation of the developed method was performed according to the ICH Q2(R1) guideline. Favorable validation parameters, such as lower limit of quantitation at the concentration level of 0.25 µg/mL, were obtained. Finally, the proposed method was applied for quantification of triptorelin in a commercial drug (Diphereline® 0.1 mg, powder for injection) sample. Applicability of the method was evaluated using the Blue Applicability Grade Index, which highlighted its superior practicality.

Keywords *capillary zone electrophoresis, therapeutic peptides, repeated sample injection*

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PREPARATION AND CHARACTERIZATION OF NANODISPERSION SYSTEMS FOR ENHANCED DELIVERY OF POORLY SOLUBLE CURCUMIN

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Abstract Curcumin, a natural compound derived from turmeric, possesses a broad spectrum of pharmacological effects, including anti-inflammatory, antioxidant, and antibacterial activities. However, due to its high lipophilicity and poor water solubility, photodegradation and pH instability result in low bioavailability and, therefore, limited therapeutic applications. One strategy to overcome these limitations and improve its therapeutic potential is the formulation of nanodispersion systems, which may enhance drug permeation and enable delivery at therapeutically relevant concentrations. Microemulsions, due to their unique physicochemical properties, represent one such promising drug delivery system. This work evaluates the properties of oil-in-water microemulsions with various oil phases and aqueous solutions of penetration enhancers (dimethyl sulfoxide and triethanolamine), prepared by the phase titration method for topical application of curcumin. Based on the physicochemical properties and the release profiles of curcumin, the most suitable formulations contained 10% w/w triethanolamine. To increase viscosity, microemulsion gels were prepared from selected microemulsions using xanthan gum, hydroxyethyl cellulose, and carbopol as gelling agents at various concentrations. The higher viscosity of these systems had a significant effect on permeation. The influence of these dispersion systems on drug release was evaluated through regenerated cellulose membranes using Franz diffusion cells. According to the results, the most suitable formulation for curcumin was a microemulsion gel containing 1% w/w hydroxyethyl cellulose, based on a microemulsion with oleic acid as the oil phase and 10% w/w triethanolamine as the aqueous phase. This formulation exhibited the highest viscosity and simultaneously the highest cumulative amount of curcumin released after 6 h. Evaluation of kinetic parameters indicated that the release of curcumin was primarily controlled by diffusion through the gel matrix, following a diffusion-based mechanism according to the Higuchi kinetic model.

Keywords *curcumin, microemulsion, gelling agent, triethanolamine*

EVALUATION OF THE WOUND-HEALING ACTIVITY OF TRANSFERSOMAL GEL CONTAINING BINAHONG LEAF EXTRACT (*ANREDERA CORDIFOLIA* (TEN.) STEENIS) FOR ACCELERATING DIABETIC WOUND CLOSURE

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Abstract Diabetes mellitus is a prevalent metabolic disorder in Indonesia. If left untreated, diabetic ulcers may progress to severe infections. One topical formulation commonly used for wound care is gel, a semisolid preparation that offers advantages such as a cooling sensation, ease of application, and non-stickiness to the skin. Vitexin, a bioactive compound found in *Anredera cordifolia* (commonly known as binahong leaves), helps prevent the progression of ulcers by activating Nrf2 and inhibiting tumor necrosis factor-α in the dermal layer. However, since vitexin is prone to degradation in the alkaline pH of wounds, transfersomes are employed to enhance its stability and facilitate deeper dermal penetration. This study aimed to investigate the wound-healing activity of a binahong leaf extract transfersomal gel in accelerating the closure of diabetic wounds. The research employed a true experimental design and received ethical clearance. The independent variable was the concentration of binahong leaf extract in the gel, while the dependent variable was the percentage of wound closure in diabetic rats. A total of 24 rats were induced with diabetes using streptozotocin, and blood glucose levels were measured using the GOD-PAP method. Diabetic ulcers were created using a 5-mm punch biopsy, after which the gel formulations were applied twice daily for 21 days. Wound closure was monitored and measured using MacBiophotonic ImageJ software, and data normality was analyzed using SPSS. The results demonstrated that the transfersomal gel containing 20% binahong leaf extract exhibited the most effective wound closure percentage. Statistical analysis revealed a *p*-value <0.05, indicating that the formulation significantly accelerated the healing of diabetic wounds.

Keywords *Diabetic wound, transfersome, Anredera cordifolia, vitexin, gel*

MECHANICAL CHARACTERIZATION OF CO-PROCESSED EXCIPIENTS USING THE COMPACTION TRIANGLE AND HECKEL MODELING IN EARLY FORMULATION DESIGN

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Abstract The development of directly compressed solid dosage forms requires excipients that exhibit adequate compressibility, compactability, and deformation behavior to ensure the integrity of the final tablet. This study presents a comprehensive mechanical evaluation of co-processed excipients using two complementary approaches: the compaction triangle and the Heckel equation.

A group of commercially available co-processed excipients with diverse compositions was tested using an instrumented single-punch compaction analyzer designed to record force–displacement profiles. The analysis followed the principles outlined in the pharmacopeial article entitled Tablet Compression Characterization. Each excipient was evaluated using the compaction triangle, which graphically integrates compressibility, compactability, and tabletability to provide a multidimensional view of compaction behavior. In addition, deformation kinetics were interpreted using Heckel modeling to describe the densification mechanism and yield characteristics of the powder beds.

The results revealed distinct compaction profiles across the excipient groups. Microcrystalline cellulose-based systems displayed resistance to densification, with gradual plastic deformation and reliable mechanical properties. Lactose-based matrices showed faster densification and lower resistance to deformation, often leading to reduced mechanical performance. Combined systems containing soluble fillers and functional binders exhibited more variable responses, with some formulations offering favorable mechanical behavior due to synergistic material properties and production methods.

This work provides a coherent mechanical profile of co-processed excipients under defined compression conditions. The combined use of the compaction triangle and Heckel modeling enables a deeper understanding of formulation behavior and facilitates the definition of design space, supporting risk-based excipient selection and robust formulation development within the principles of Quality by Design.

Keywords *Co-processed excipients, Tablet Compression Characterization, compaction triangle, Heckel analysis*

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PHARMACEUTICAL FORMS OF OVER-THE-COUNTER DRUGS

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Abstract Over-the-counter medicine is also known as OTC or nonprescription medicine. All these terms refer to medicine that is possible to buy without a prescription. In our work, we monitored the representation of different pharmaceutical forms of OTC drugs in global, European, US, and veterinary global markets. The global OTC drugs market was valued at USD 180 billion in 2024. The tablets segment leads the market accounting for the highest market revenue of USD 85.9 billion in 2024 and is projected to reach USD 138.4 billion by 2034. The next best-selling pharmaceutical forms are liquids, ointments, and in the fourth place are sprays. The European OTC drugs market is valued at USD 36.6 billion in 2025. By formulation, tablets and caplets accounted for 47.8% of the European OTC Drugs market size in 2024, while gummies, lozenges, and dissolvable films are advancing at an 11.4% Compound Annual Growth Rate (CAGR) to 2030. The United States OTC Drugs Market size is estimated at USD 44.68 billion in 2025. Due to its stability and convenience in packaging, shipping, and dispensing, tablets are the best-selling pharmaceutical forms. The global OTC Veterinary Drugs Market has gained immense growth throughout the world in recent times. Oral medications, including chewable tablets and liquid formulations, remain the most widely used. Injectable drugs are often preferred for quick relief and long-lasting effects. Topical treatments, for example, spot-on solutions and medicated shampoos, offer external relief for dermatological and parasitic issues. Powders and sprays are gaining popularity for niche applications. In conclusion, solid dosage forms, for example, tablets, form the largest part of the OTC drugs market due to their ease of administration and enabling the easiest and most accurate dosing of the drug. In conclusion, solid dosage forms such as tablets dominate the OTC drugs market due to their ease of administration and their ability to provide the most convenient and accurate dosing of medication.

Keywords *OTC drugs, pharmaceutical forms*

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AUTOOXIDATION-INDUCED STRUCTURAL ALTERATIONS OF EXOGENOUS PULMONARY SURFACTANT

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Abstract The pulmonary surfactant is a complex mixture of lipids and proteins that reduces surface tension within the alveoli, minimizing the work of the body during breathing. Oxidative stress can markedly affect its function. We investigated structural alterations of porcine-derived pulmonary surfactant (Curosurf®) induced by autooxidation. Oxidation was initiated by exposing freshly opened Curosurf® samples to ambient air and incubating them at 37 °C for up to 7 days. The level of oxidation of the phospholipids was followed through oxidation index as the ratio A_{233}/A_{210} (UV–VIS). Synchrotron small-angle X-ray scattering of fresh Curosurf® shows two lamellar phases with repeat distances *d* ~ 10.2 and 11.6 nm, superposed to a broad background characteristic for uni- and/or oligo-lamellar vesicles. The *d* value of both phases decreases with increasing temperature, and a gel-to-fluid phase transition was detected at Tm ~28°C. However, oxidized Curosurf® exhibited a single lamellar phase at 20°C with *d* ~ 8.0 nm, transitioning to the fluid state at *Tm*~ 40°C. Structural changes manifested by the increasing intensity and narrowing of the peaks and flattening of the background indicate a well-organized lamellar phase. Thus, oxidation resulted in the reduction of uni- and oligo-lamellar vesicles. Both evident structural changes, coupled with an elevated *Tm*, may impair the response efficiency of the surfactant during inhalation. Our findings contribute to a deeper understanding of the mechanism by which oxidative stress inhibits pulmonary surfactant function.

Keywords *pulmonary surfactant, autooxidation, SAXS/WAXS*

Acknowledgment Small-angle X-ray scattering*/wide-angle X-ray scattering WAXS experiments were performed at Alba synchrotron with the help of the staff. The research was supported by VEGA 1/0305/24.*

LIPOSOMES – POTENTIAL CARRIERS OF THE ANTIVIRAL AGENT GC376

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Abstract Coronaviruses are serious pathogens capable of causing large-scale epidemics and pandemics. Despite their clinical significance, therapeutic options remain limited. GC376 has emerged as a promising antiviral candidate targeting the 3-chymotrypsin-like protease (3CLpro), an enzyme essential for viral RNA replication and transcription. Inhibition of this protease disrupts the viral life cycle, making 3CLpro an attractive target for the development of specific antiviral agents. While GC376 demonstrates potent antiviral activity, its interactions with biological membranes are not sufficiently characterized, despite their substantial influence on key pharmacokinetic properties. Understanding drug–lipid interactions is thus essential for designing efficient drug delivery systems. The lipid–water partition coefficient (K_p) is a key parameter reflecting distribution of a compound between the aqueous and lipophilic phases, offering valuable insight into membrane affinity and biological potential. In this study, we investigated the physicochemical behavior of GC376 in lipid systems composed of unilamellar liposomes prepared from the thermosensitive phospholipid 1,2-dipalmitoyl-*sn*-glycero-3-phosphatidylcholine (DPPC) dispersed in 150 mmol/L NaCl. The partition coefficient K_p was determined using UV–VIS spectrophotometry by monitoring GC376 absorption maxima at $\lambda = 257$ nm in a series of samples at a constant GC376 concentration and increasing lipid concentration. Measurements were performed at 25°C, 37°C, and 50°C, corresponding to the gel (L_b), ripple-gel (P_b), and fluid phases (L_a) of DPPC, respectively. In addition, dynamic light scattering was used to assess liposome size and homogeneity and electrophoretic light scattering was used to evaluate their surface charge and colloidal stability. Results indicate that the affinity of GC376 for lipid bilayers increases with temperature, with $K_p^{Lb} < K_p^{Pb} < K_p^{La}$. These findings support the potential use of liposomes as temperature-responsive carriers for GC376 and contribute to a better understanding of its membrane interactions, which are critical for optimizing antiviral drug delivery strategies.

Keywords *GC376, lipid bilayer, partition coefficient*

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PREPARATION OF MONOCLONAL ANTIBODY TOCILIZUMAB FOR INHALATION DELIVERY ROUTE

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Abstract Biopharmaceuticals (including monoclonal antibodies, therapeutic peptide, oligonucleotides, or peptide conjugates) are typically delivered to the organism by intravenous, subcutaneous, or intramuscular application route. However, such delivery routes do not possess suitable safety profile, especially in cases of diseases affecting the respiratory tract. Inhalation delivery route is a noninvasive technique allowing administration of drugs both locally and systematically. However, some procedures described in recent scientific papers led to a progress in development of drugs delivered by such way, the appropriate procedures for formulation of biopharmaceuticals applied via inhalation are still not well characterized and understood. Development of such drug formulations also demands appropriate analytical methods for their quality control to ensure safety and efficacy.

In present work, four tocilizumab formulations for inhalation were prepared in different formulation buffers composed of 1) phosphate-buffered saline, 2) histidine with arginine (His + Arg), 3) proline (Pro), and 4) glycine with NaCl (Gly + NaCl). The stability of the monoclonal antibody (mAb) (at the concentration level of 1 mg/mL) in such formulation buffers was investigated. The formulated mAb solutions were incubated at −80°C, −20°C, and 4°C for 24 h and at 60°C for 2 h, and then the formulations were analyzed by size exclusion chromatography (SEC) to investigate the presence of aggregates. Tocilizumab showed appropriate stability in formulated buffer under such tested conditions. Tocilizumab formulated in the Pro buffer at pH 5.8 was used for pivotal testing of nebulization procedure. No significant formation of aggregates was observed after the nebulization procedure. The obtained results create a good starting point for further development of monoclonal antibodies applicable by inhalation route.

Keywords *tocilizumab, monoclonal antibody, inhalation delivery route, nebulization*

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DESIGN OF DRUG DELIVERY SYSTEMS DERIVED FROM MICROALGAE

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Abstract Nanodelivery systems offer versatile applications for a wide range of biologically active compounds. However, the search for biosources that are freely available and meet environmental and sustainability criteria is becoming increasingly relevant. Cell membrane–derived carriers, known as ghost vesicles (GVs), mimic the complexity of natural proteolipid biomembranes and represent a new platform in drug delivery. The unicellular marine microalga *Dunaliella tertiolecta* (DT) has been shown to be a suitable cell model for the preparation of GVs. DT-derived GVs do not show significant cytotoxicity or induce a systemic immune response. On the contrary, they contain numerous bioproducts with proven bioprotective activity, what broadens their therapeutic potential.

We determined basic physicochemical parameters of DT-derived GVs, such as vesicle size, size distribution, lamellarity, and antioxidant activity, which are known to affect vesicle stability, internalization by cells, and the efflux rate of the encapsulated drug. Furthermore, we investigated the applicability of DT-derived GVs as carriers for biomacromolecular drugs, DNA, and bovine serum albumin, employing the technique of fluorescence spectroscopy. Our results indicated that DT-derived GVs might expand the repertoire of nanodelivery systems for therapeutic biomacromolecules.

Keywords *drug delivery systems, sustainable resources, microalgae, macromolecular drugs*

ASSESSMENT OF MUCOADHESIVE PROPERTIES OF OROMUCOSAL PREPARATIONS

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Abstract Oromucosal preparations are dosage forms classified as oral medications, administered into the oral cavity for a local or systemic effect. The specific site of drug absorption is the inner side of the buccal mucosa. The advantage is the rapid absorption of systemically acting drugs, which bypasses the first-pass effect and allows for the incorporation of drugs susceptible to degradation in the gastrointestinal tract. Oromucosal preparations are also an important dosage form in the management of oral cavity inflammation. In this case, locally acting drugs are administered, and it is therefore desirable that the dosage form remains on the buccal mucosa for as long as possible. It follows from the above that not only the efficacy of buccal drugs for oral cavity inflammation but also patient compliance with buccal drugs is influenced by their degree of mucoadhesion. Mucoadhesivity is the ability of a drug form to adhere to the mucosa through several mechanisms. Its purpose is to prolong the contact of the drug form with the mucosa to create optimal conditions for the drug to be effective. Given the importance of this property of buccal medications, basic research must be able to objectively assess mucoadhesion of a drug form. The main objective of this study is to evaluate the effectiveness of methods for measuring mucoadhesiveness *in vitro* and *ex vivo*, to define their possible correlation, and to discuss their potential use in the development of oromucosal preparations. Buccal tablets were chosen as the model dosage form. Texturometric methods using natural and synthetic buccal mucosa were evaluated in the context of swelling kinetics. Certain correlations between swelling and mucoadhesion were found, with statistically significant results.

Keywords *mucoadhesivity, texturometry, swelling kinetics, buccal mucosa, tablets*

ORALLY DISINTEGRATING TABLETS CONTAINING LINDEN EXTRACT (*TILIA PLATYPHYLLOS* SCOP.) PREPARED BY THE VOLATILE SUBSTANCE COMPRESSION METHOD

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Abstract Extract from *Tiliae flos* (*Tilia platyphyllos* Scop.) exhibits mucoprotective and anti-inflammatory effects due to its mucilage and flavonoid content when administered orally. Orally disintegrating tablets (ODTs) are ideal for delivering this extract, as they rapidly disintegrate in the mouth without water, allowing immediate release of active ingredients. ODTs are characterized by high porosity, achievable through methods such as compression of a volatile substance into tablets followed by sublimation. This study aimed to evaluate the effects of linden extract concentration (5%, 10%, or 20%) and extraction solvent type (ethanol or water) on the physicomechanical properties of tablet blend and resulting ODTs prepared by compressing volatile camphor (20% w/w). The ODTs produced were lens shaped, 11 mm in diameter, and weighed 400 ± 10 mg after camphor removal. Sieve analysis showed median particle sizes between 65 and 67 µm for all samples. Flow properties were assessed by flow time (3–20 s), angle of repose (25°–30°), Hausner ratio (1.12–1.23), and compressibility index (10%–18%), indicating average to good flowability. The ODTs demonstrated acceptable wetting times (1–13 s) and disintegration times (14–52 s), but exhibited relatively high friability (2%–18%). Statistical analysis using Pearson correlation and mixed analysis of variance revealed that increasing the extract content significantly raised bulk density ($p < 0.05$) and prolonged wetting time ($p < 0.001$). The extraction solvent significantly influenced ODT friability ($p < 0.001$), and higher extract amounts increased tablet height ($p < 0.05$). The batch with 20% extract, 10% Avicel® PH-101, 49% mannitol, 20% camphor, and 1% talc showed the best physicomechanical properties, making it the most suitable formulation for orally dispersible linden extract tablets.

Keywords *lime tree, extraction, camphor, sublimation, flow properties*

DETERMINATION OF SUN PROTECTION FACTOR AND SENSORY ANALYSIS OF PHOTOPROTECTIVE CREAMS

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Abstract The study presents the preparation, comprehensive evaluation, and stability analysis of novel photoprotective sunscreen formulations. Four distinct formulations were developed, each containing organic ultraviolet (UV) filters (Eusolex® 2292, Eusolex® OS, Tinosorb® M, and Tinosorb® S) and varying primarily in the type of emulsifier used – Polysorbate® 80 or Span® 80 – as well as the inclusion of the inorganic UV filter zinc oxide. The primary objectives were to determine the sun protection factor (SPF) using a spectrophotometric method and to assess the formulations' physical properties through rheological and textural analyses. Stability was rigorously evaluated using freeze-thaw cycling and centrifugation tests to assess resistance to phase separation. While the formulation containing Span® 80 (F3) exhibited the highest SPF, the Polysorbate® 80-based formulation (F1) demonstrated superior stability under stress conditions. Sensory analysis with a small group of volunteers provided valuable subjective feedback on texture, spreadability, and overall feel for F1 and its zinc oxide-enriched counterpart (F2). The results indicate that modifications in emulsifier type significantly influence SPF, physical characteristics, stability, and user perception of sunscreen products. These findings offer important insights for the development of effective, stable, and consumer-friendly photoprotective formulations.

Keywords *sun protection factor, Polysorbate® 80, Span® 80, stability testing, sensory analysis*

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PHARMACEUTICAL PROMISES OF BENZOFURAN DERIVATIVES: SYNTHETIC DEVELOPMENT AND *IN SILICO* EVALUATION OF SKIN PERMEATION

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Abstract Benzofuran-based structures represent an exceptional class of heterocyclic compounds renowned for their diverse biological activities, thereby rendering them highly valuable in pharmaceutical research. This study focused on the design and synthesis of novel benzofuran-derived molecules as well as their *in silico* evaluation in order to predict the potential to permeate *stratum corneum*. These (5-chlorobenzofuran-2-yl) (4-substituted piperazin-1-yl)methanones were prepared *via* a two-step synthetic process. Their structures were verified using relevant spectral methods (nuclear magnetic resonance and infrared; ^{1}H-NMR and IR). For the final derivatives, retention factor values from thinlayer chromatography, melting points, and solubility in selected solvents, namely water, methanol, ethanol 96%, and dimethyl sulfoxide, were determined. The ability of the desired compounds to passively cross *via stratum corneum* was predicted using three well-established *in silico* models developed by Potts and Guy, Cronin, and Barratt. These computational approaches generally facilitate the experimental determination of the permeability coefficient (k_p) or its logarithmic counterpart (log k_p), thereby offering insights into the probability of compounds´ transdermal penetration. The observed findings and conclusions could be utilized as the fundamental platform for the design and pharmacological evaluation of a wide palette of benzofuran derivatives with promising potential for pharmaceutical application.

Keywords *benzofuran, in silico, skin permeation*

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STUDY OF THE EFFECT OF CHONDROITIN SULFATE AND FUCOIDAN ON THE BLOOD COUNT OF LABORATORY MICE

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Abstract Immunotherapeutic approaches have been supported by the discovery of a specific serum Gc-globulin with the ability to convert to a specific globulin component of macrophage activating factor (GcMAF). GcMAF plays the role of a regulatory glycoprotein involved in the body's defense mechanisms through the activation of macrophages, tumoricidal effects directed against malignant cells, as well as by enhancing other biological processes of the immune system. Nagalase deglycosylates *N*-acetylgalactosamine from the GcMAF molecule, thereby inactivating the protein and leading to the disappearance of several signaling mechanisms of the immune system. We experimentally administered 2 million Hepa1c1c7 tumor cells subcutaneously to BALB/c mice and applied perorally substances chondroitin sulfate (CS), fucoidan (F), and their combination CS + F. We studied the effects of the oral drug on the immune response of Hepa1c1c17-infected mice by determining the number of leukocytes and the percentage of individual leukocyte forms. A decrease in total leukocyte count was observed between the first collection (three doses) and the third collection (13 doses) for the administered substances CS, F, and CS + F. From the differential blood count, we observed a decrease in lymphocytes, but at the same time an increase in neutrophils within the percentage values for a healthy mouse. Our results are original; substances CS and F were tested by us for the first time in an *in vivo* model of laboratory mice. From the obtained results, we can tentatively conclude that the substances studied by us did not show any toxicity in laboratory mice after they were oral administered. Confirmation of the promising effects of the studied substances may represent an important direction within the framework of GcMAF immunotherapy.

Keywords *chondroitin sulfate, fucoidan, laboratory mice, differential blood count*

Acknowledgment *This work was supported by funding from the Slovak Scientific Grant Agency (VEGA 1/0146/23).*

INVESTIGATION OF THE EFFECT OF TEMPERATURE ON PHYSICOCHEMICAL PARAMETERS OF MICELLIZATION OF SURFACTANT – UNDECYL TRIMETHYLAMMONIUM BROMIDE IN AQUEOUS SOLUTION BY THREE EXPERIMENTAL TECHNIQUES

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Abstract Surfactants are most versatile chemicals, with an amphiphilic molecular structure, capable of forming aggregates (micelles). Micellization is a cooperative process that is demonstrated by critical micellar concentration (CMC), which is defined as the minimal concentration of the surfactant at which micelles begin to form. Studying the thermodynamics of micellization is essential to understand the interactions that control the micellization process. Important thermodynamic parameters describing micellization are the standard molar Gibbs energy, enthalpy, and entropy of micellization and are determined from changes in CMC with the temperature. This study presents the results of the conductometric, densitometric, and spectrophotometric measurements of aqueous solutions undecyl trimethylammonium bromide (UTMABr), a surfactant with an atypical number of carbons in the hydrocarbon chain This study presents the results of conductometric, densitometric, and spectrophotometric analyses of aqueous solutions of undecyl trimethylammonium bromide (UTMABr), a surfactant with an unusual hydrocarbon chain length - 11 (usually surfactants with an even number of carbons in the chain are studied) at 25°C–50°C and in concentration range (23–42)× 10^{-3} mol/dm^3. The measured values are increased by increasing the UTMABr concentration and the temperature of the solutions. CMC values have been calculated for all experimental techniques, using four computing procedures (conventional, first and second derivatives, and integration). The average CMC values are from the interval (32.11–33.41)× 10^{-3} mol/dm^3 with small standard deviations. CMC versus temperature dependence increases in a nonlinear fashion. Thermodynamic quantities of micellization were calculated from the average value of CMC. All of them decreased with temperature, which characterize a spontaneous and exothermic process of micellization. Examination of micellization parameters of commercial and synthesized surfactants is an important factor for their applications.

Keywords *tenside, critical micellar concentration, thermodynamical parameters of micellization*

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ANALYTICAL STRATEGIES FOR CHARACTERIZATION OF KEYHOLE LIMPET HEMOCYANIN

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Abstract Keyhole limpet hemocyanin (KLH) is an extracellular respiratory protein which is obtained from the Californian giant keyhole limpet *Megathura crenulata*. The KLH protein consists of two structurally and physiologically distinct isoforms, KLH1 and KLH2, each based on a subunit with molecular weight of approximately 400 kDa. This protein acts as a potent immunoactivator, and therefore, it is widely used as hapten carrier and immune stimulant in research and clinical studies. Exact characterization of KLH alone or in position of a carrier protein is necessary from the quality and efficiency point of view. Moreover, knowledge of exact concentration of carrier proteins and/or conjugated peptide in such vaccines is very important not only from regulatory but also from clinical point of view. Information about the concentration of therapeutic peptide/protein can be used to adjust the effective and safe dose. Similarly, information about the concentration of the carrier protein is necessary for quality assurance of pharmaceutical ingredients. However, the knowledge about properties of KLH is more than 20 years old and there are still missing appropriate analytical strategies for its detail characterization. The present work deals with the implementation of various analytical strategies based on size exclusion chromatography, amino acid analysis, peptide profiling (mapping), or *N*-glycan analysis in the field of characterization of KLH.

Keywords *liquid chromatography, mass spectrometry, carrier protein, biologics, quality control*

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VETERINARY EYE DROPS WITH A BIOLOGICAL COMPONENT

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Abstract Mesenchymal stem cells are widely used in tissue engineering. Their advantage is high proliferative potential (ability to multiply) and pluripotency, that is, the ability to differentiate into cells of multiple tissue lineages and secrete molecules that activate other cells at the site of damage. They thus participate in the modulation of the inflammatory process, which accelerates regeneration. In production of tissue cultures, a significant component is the conditioned medium containing nutrients for the cells. After a certain time, the medium is replaced with fresh medium, while the used medium contains cell secretions (secretome) with several biologically active substances (growth factors, cytokines, extracellular vesicles, e.g., exosomes, lipids, proteins, nucleic acids, and metabolites). In addition to the cultures themselves, such conditioned medium is also used in tissue therapy and regeneration. The amount of biologically active substances in the medium varies depending on the length of time the conditioned medium is in contact with tissue culture. These biologically active substances influence tissue healing processes, suppress inflammation, protect cells from apoptosis, stimulate angiogenesis, and regenerate nerve tissue. They are shown to be a cell-free therapeutic alternative with a reduced risk of post-transplant reactions. Eye drops were prepared according to the composition proposed by Biom-R (Dr. Kubeš) as part of the Memorandum of Cooperation between Biom-R and the Faculty of Pharmacy, Comenius University. Eye drops according to the proposed composition developed by Biom-R (Dr. Kubeš) within the framework of the Memorandum of Cooperation between Biom-R and the Faculty of Pharmacy, Comenius University were prepared. The supplied conditioned medium was from stem cell propagation. In the experiments, the composition of the proposed drops was slightly modified and possibilities of aseptic preparation using bacterial filtration were verified. After adjusting pH to accepted physiological range, physicochemical properties (viscosity, surface tension, and density) and *ex vivo* irritancy on erythrocytes were evaluated. Samples containing preservative and those without preservatives were compared; the lowest hemolysis was observed in samples without preservatives. Single-dose packaging was chosen as a suitable solution.

Keywords *eye drops, density, surface tension, viscosity, irritancy*

PARACETAMOL – ITS DETERMINATION IN SUPPOSITORIES BY UV/VIS SPECTROPHOTOMETRY

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Abstract The thesis focuses on the development of a methodology for the determination of paracetamol in suppositories, which are prepared in pharmacies and must comply with the conditions specified in the Pharmacopoeia. The subject of the analysis was suppositories prepared in a pharmacy, each containing 500 mg of paracetamol; hard fat was used as the excipient. Ultraviolet/visible (UV/VIS) absorption spectrophotometry was employed for the determination of paracetamol in the suppositories. Two sample preparation methods were developed in this study: A) Preparation of an aqueous sample solution at elevated temperature with the addition of sodium hydroxide, followed by filtration and dilution of the filtrate and B) preparation of an aqueous sample solution at elevated temperature, followed by cooling to 5°C, removal of hard fat by filtration, and subsequent dilution of the filtrate. The prepared sample solutions and standard solutions were measured using a Shimadzu UV-1800 spectrophotometer with Shimadzu UV Probe software. Based on the absorbance data of the standard solutions, the specific absorbance was calculated, and the linearity of the paracetamol determination was verified using the calibration curve method. The obtained data were evaluated statistically. The paracetamol content determined using method A was 95.98% ± 0.49%, while method B yielded 95.61% ± 0.68%. The results obtained by UV/VIS spectrophotometry using both sample preparation methods were compared to those obtained by volumetric analysis, in accordance with the Pharmacopoeia monograph *Paracetamol*. A 0.1 M solution of $(NH_4)_2Ce(NO_3)_6$, the automated burette *Titrette*, and ferroin as an indicator were used for the volumetric determination. The paracetamol content in the suppositories determined by this method was 97.42% ± 1.00%. All determined paracetamol contents were within the acceptable limits for content uniformity in single-dose preparations, as specified by the European Pharmacopoeia for this dosage form.

Keywords *paracetamol, suppositories, UV/VIS spectrophotometry, volumetric analysis*

THE ROLE OF PHARMACIES IN EXTEMPORANEOUS PREPARATION

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Abstract In the healthcare system and its provision, pharmacies, as professional and consulting workplaces, have an irreplaceable position. The transition to individualized healthcare, regarding the needs of the patient as an individual, is a challenge for today's society. It is, therefore, important to apply these requirements also to the revival of magistral preparation and to move from its obsolete forms to innovative possibilities within the framework of cooperation between a public pharmacy and a doctor. The pharmacist at our health center becomes a mediator of expertise between the doctor and the patient. The pharmacist provides doctors with consultations regarding technology and the possibilities of incorporating medicines, maintaining a compatible preparation, and helps the patient by explaining the application, thereby reinforcing patient compliance, all in accordance with the Good Pharmacy Practice (GPP) . Since centralized preparation is not legally permitted in Slovakia, every pharmacy struggles with the issue of economic management when writing off and disposing of expired raw materials. Therefore, cooperation between the pharmacist and doctors must be at a high professional and economic level, with the primary goal of achieving a positive outcome for individualized patient therapy. The solution for a public pharmacy located in a health center to provide complete healthcare, including magistral preparation, relies on professional communication with the possibilities and innovations in technological preparation. This includes developing an individual approach regarding a doctor's specialization. Within the pharmacy network, we are introducing the possibility of educating about magistral preparation in the form of professional articles, providing consultations to other pharmacies, and through online lectures.

Keywords *extemporaneous preparation, individualized therapy, pharmacy, physician–pharmacist cooperation in Slovakia*

DEVELOPMENT OF LIQUISOLID SYSTEMS FOR IMPROVED DISSOLUTION RATE OF TADALAFIL

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Abstract Preparing liquisolid systems (LSS) represents an innovative approach to addressing the limited aqueous solubility of orally administered drugs such as tadalafil. LSS are formulated by dispersing the drug in a hydrophilic, non-volatile solvent and incorporating it into a porous carrier. However, selecting suitable excipients, particularly an appropriate non-volatile solvent, is crucial as it significantly impacts the overall drug release behavior and formulation performance. For this reason, the presented study evaluated the effect of tadalafil concentration (2.5%, 5%, and 10%) and dispersion type on the drug release rate from LSS. Moreover, the effect of surfactant addition on drug dispersion type (solution or suspension) and dissolution behavior has been investigated.

All prepared LSS formulations significantly improved drug release compared to pure tadalafil, which can be attributed to the distribution of the drug dispersion over the carrier surface, thereby increasing its accessibility to the dissolution medium. Furthermore, the results indicate that the lower the drug concentration in the adsorbed dispersion, the faster the release from the final LSS. This effect is closely related to the dispersion type, with the 2.5% dispersion existing as a solution, while the 5% and 10% dispersions were in the form of suspensions.

Although LSS containing 2.5% tadalafil solution showed promising improvements in drug release, the amount of LSS powder corresponding to a 5 mg drug dose was 400 mg. Such an amount of LSS powder would be challenging to process into tablets that remain easily swallowable for patients. For this reason, the 0.5% solutions of surfactants (sodium lauryl sulfate and cetyltrimethylammonium bromide) in polyethylene glycol 300 were used as non-volatile solvents to obtain tadalafil dispersion. However, the inclusion of surfactants did not affect the dissolution performance, demonstrating that their presence did not further enhance the drug release.

Keywords *tadalafil, liquisolid systems, mesoporous silica, enhanced dissolution, Neusilin® US2*

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FORMULATION OF STIMULI-RESPONSIVE GELS CONTAINING SILVER COMPLEX WITH NICOTINAMIDE

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Abstract The use of stimuli-responsive gels is increasingly widespread and includes almost all routes of administration. Their main property is the phase transition from sol to gel under the influence of physiological stimuli such as temperature, pH, ion presence, or enzymes. The aim of this formulation study was to prepare oral *in situ* gel containing silver complex with nicotinamide. We prepared formulations based on the thermosensitive polymer Pluronic® F-127 (15% w/w), methylcellulose (0.25% w/w), and various concentrations of the ion-sensitive polymer sodium alginate (0.2%–4% w/w). Various properties were evaluated, such as pH, injectability, and critical sol–gel transition temperature of sols, gelation capacity, as well as dissolution profile and antimicrobial activity. We found that sodium alginate affects the critical sol–gel transition temperature of sols, and with higher concentrations, the sol–gel transition temperature decreases. At a 4% w/w sodium alginate concentration, the presence of calcium cations was necessary for gel formation. Sodium alginate also significantly influenced the viscosity of sols; higher concentrations led to more viscous sols. The most suitable formulation contained 4% sodium alginate and was used to incorporate silver complex with nicotinamide, a new potential antimicrobial agent. The drug release kinetics most closely correlated with first-order kinetics, and the drug was released via Fickian diffusion. During antimicrobial activity testing, the formulation demonstrated higher efficacy against *Pseudomonas aeruginosa* compared to a commercial dental gel containing chlorhexidine gluconate, although this difference was not statistically significant. Overall, the chlorhexidine gel showed greater efficacy against most of the tested bacteria, while the antimicrobial *in situ* gel maintained a consistent moderate level of antimicrobial activity.

Keywords *in situ gels, silver nicotinamide, sodium alginate, methylcellulose, poloxamer*

BLOOD–BRAIN BARRIER TRANSPORT SYSTEM FOR THERAPY AND DIAGNOSIS OF NEURODEGENERATIVE DISEASES

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Abstract Alzheimer's disease (AD) is characterized by presence of insoluble aggregates of hyperphosphorylated tau proteins (1,2). Several therapeutic monoclonal antibodies (mAbs) have been approved for clinical use; their efficacy is limited by the blood–brain barrier (BBB), restricting their passage due to its selective nature (3,4). In this study, we aim to develop a single-chain variable fragment (scFv) with binding affinity to surface receptor proteins of rat endothelial cells, such as low-density lipoprotein receptor-related protein 8 (LRP8) or angulin-1, facilitating receptor-mediated transcytosis for improved BBB penetration. The recombinant LRP8 and angulin-1 proteins were produced using mammalian cell expression system and were used to immunize mice to generate mAbs. mAbs were fragmented to produce scFv. Specificity and efficacy of the antibodies were evaluated using western blotting, enzyme-linked immunosorbent assay, immunostainings, and flow cytometry. BBB transcytosis of the antibodies was analyzed using an *in vitro* 2D-BBB model. We have successfully produced a LRP8 receptor-specific scFv, significantly recognizing primary rat endothelial cells and capillaries in rat brain tissue as shown in rat endothelial and brain capillary staining. Permeability experiments demonstrated that scFv crosses BBB. Through this study, we aim to develop an efficient drug delivery system capable of crossing the complex BBB, which can also serve as a diagnostic tool for detecting tau pathology. In addition, we will assess the permeability of the LRP8-specific scFv in transgenic rat model for tauopathy. Furthermore, we will evaluate the ability of the generated scFv to recognize tau pathology in the brain tissue.

Keywords *Alzheimer´s disease, blood–brain barrier, tau, antibodies*

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