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PHARMACEUTICAL SCIENCES: INTERNATIONAL SCIENTIFIC CONFERENCE ON MEDICINE AND HEALTH SCIENCES OF THE UNIVERSITY OF LATVIA, 2026

On 26 April 2026, the University of Latvia, in Rīga, hosted the International Scientific Conference on Medicine and Health Sciences.

The "Pharmaceutical Sciences" section presented diverse, interdisciplinary research addressing complex healthcare challenges, including drug formulation, preclinical and clinical studies, adverse effects, *in vitro* disease modelling, and gene polymorphisms. Contributions from Latvia, Lithuania, and India highlighted strong international collaboration.

In the domain of preclinical drug studies, the abstracts provided insights *in vitro* models of NAFLD and Parkinsons disease. Findings supported the hepatoprotective potential of anti-diabetic drugs and highlighted their promise as therapeutic agents in NAFLD. The studies on anti-Parkinsonian effects of selected polyphenols in *in vitro* PD models were focused on DA metabolism and αSyn aggregation. The obtained data indicated that polyphenols function as multifunctional agents targeting key neurodegenerative processes in PD by inhibiting MAO-B activity and suppressing toxic αSyn aggregation. Further research is needed on 20S proteasome modulation in neuroprotection.

Research on *Silybum marianum* examined phenolic metabolites and key enzymes involved in biosynthesis across growth stages, providing insight into plant biochemical composition.

Addressing antimicrobial resistance, 74 bacterial strains were isolated from Latvian wooded dunes, including 23 *Streptomyces* strains. Several extracts showed activity against Gram-positive pathogens such as *Staphylococcus aureus* and *Bacillus subtilis*, identifying promising natural product candidates for novel antimicrobial compounds.

A retrospective study (2019–2025) of psoriasis patients treated with biological therapies (adalimumab, ustekinumab, secukinumab or risankizumab) confirmed improved disease control but highlighted the need to further evaluate laboratory-defined adverse effects, such as liver enzyme elevation and neutropenia.

In multiple sclerosis research, proteasome gene polymorphisms and vitamin D pathway genetics showed therapy-specific associations with "no evidence of disease activity" (NEDA), supporting gene–treatment interaction and personalised therapy approaches.

Advances in drug formulation include stabilisation of amorphous empagliflozin using electrospun nanofibres, offering a sustainable method to improve drug solubility. Cocrystallisation studies identified new crystalline phases, aiding solid-form optimisation of active pharmaceutical ingredients.

Innovations in drug delivery show that semi-solid extrusion 3D printing enhances transdermal menthol delivery compared to conventional methods, while also influencing key quality attributes of pharmaceutical films.

Finally, research on haemostatic materials demonstrated that Prussian blue-clay composites affect coagulation behaviour, indicating potential applications in contaminated environments.

Overall, this section highlights the integration of pharmaceutical manufacturing, biomedical research, and clinical studies, emphasising the development of innovative drugs and delivery systems for improved healthcare outcomes.

Ruta Muceniece
Zane Dzirkale

FORMULATION AND STABILISATION OF AMORPHOUS EMPAGLIFLOZIN IN CORE-SHELL ELECTROSPUN NANOFIBRES FOR ENHANCED DRUG PERFORMANCE

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Background. In line with green chemistry principles, amorphous drug formulations are favoured due to their higher solubility, enabling therapeutic efficacy at reduced dosages. Furthermore, nanofibrous drug carriers significantly enhance dissolution rates, contributing to improved bioavailability and reduced environmental impact [1].

Aim. This study investigates the stabilisation of amorphous empagliflozin (EMPA) — a selective sodium-glucose cotransporter 2 (SGLT2) inhibitor — using coaxial electrospinning to produce core-shell nanofibres.

Methods. The core polymer, *Soluplus*, was combined with a solvent system of ethanol and DMSO to dissolve empagliflozin, while *Kollicoat* was employed as the shell polymer.

Results. The amorphous nature of the resulting solid dispersions was confirmed using X-ray powder diffraction (XRPD) and morphological characterisation via scanning electron microscopy (SEM) revealed smooth, continuous fibres (Fig. 1). Differential scanning calorimetry (DSC) was used to construct two component melt phase diagrams of EMPA with selected polymers — prepared to determine the dissolution limit of EMPA, it was investigated as a function of time and EMPA concentration was quantitatively determined by UV/Vis spectroscopy and HPLC.

The electrospun nanofibres effectively inhibited recrystallisation and provided protection against UV-induced and thermal degradation.

Conclusion. This work demonstrates a promising, sustainable approach to enhancing poorly water-soluble drug delivery using electrospun nanofibre technology.

Acknowledgements

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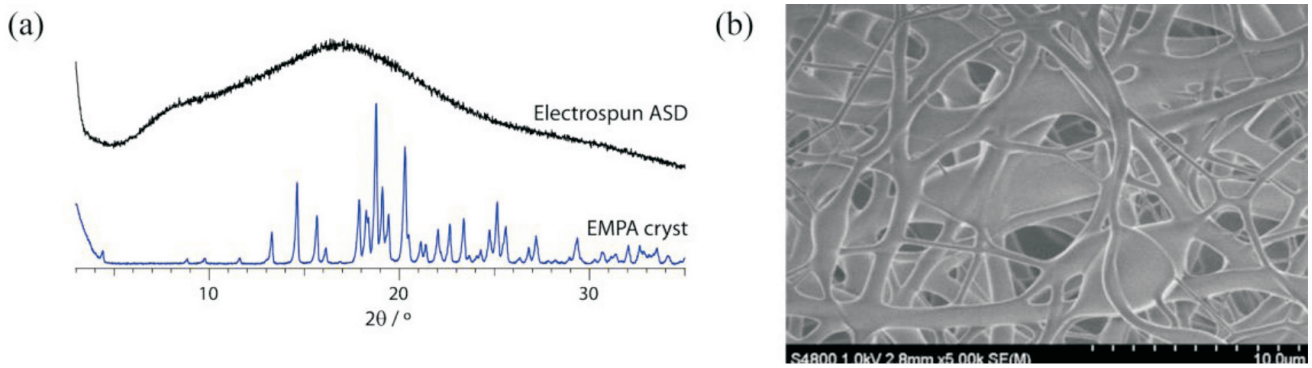

Fig. 1. (a) XRPD of electrospun amorphous solid dispersion (ASD) and crystalline EMPA, (b) SEM micrograph of the obtained electrospun ASD.

HAEMOSTATIC EFFECTS OF PRUSSIAN BLUE -CLAY COMPOSITES ON THE INTRINSIC PATHWAY: A ROTEM® INTEM EVALUATION

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Background. In CBRNE (chemical, biological, radiological, nuclear, or explosive) incidents, rapid control of bleeding is essential for survival, necessitating the development of haemostatic materials that remain effective in chemically and biologically contaminated environments. The activation of the intrinsic coagulation pathway through surface interactions is a key mechanism underlying the haemostatic properties of mineral-based biomaterials. Kaolin is a well-known activator of coagulation factor XII and is widely used in coagulation diagnostics. In contrast, montmorillonite (bentonite) exhibits a higher specific surface area and ion-exchange capacity, which may enhance its biological interactions. Although Prussian blue (PB) is generally regarded as biologically inert, its incorporation into clay-based composites may alter surface–blood interactions and influence coagulation behaviour.

Aim. The aim of this study was to evaluate and compare the effects of PB–kaolin and PB–montmorillonite composites on intrinsic pathway-mediated coagulation using viscoelastic ROTEM® INTEM testing.

Methods. *In vitro* coagulation analyses were performed using ROTEM® INTEM assays. Clotting time (CT), clot formation time (CFT), alpha angle (α), and maximum clot firmness (MCF) were determined and compared between control samples, individual materials (kaolin, montmorillonite, and PB), and the corresponding PB–clay composites.

Results. The PB–kaolin composite caused a marked reduction in CT, indicating strong activation of the contact pathway; however, this effect was accompanied by prolonged CFT, suggesting impaired clot propagation. In contrast, montmorillonite-containing samples demonstrated a more balanced coagulation response, with CT values comparable to the control and stable clot development, reflected by physiological CFT and MCF values. Pristine PB did not induce coagulation activation and was associated with prolonged clotting time (CT), confirming its lack of intrinsic procoagulant activity.

Conclusion. The observed results demonstrate that the coagulation behaviour of the composite materials is governed by synergistic surface interactions rather than by the individual properties of their constituent components. PB acts as a functional modulator of the haemostatic activity of clay minerals within composite systems. Montmorillonite-based composites promote controlled activation of the intrinsic coagulation pathway, whereas kaolin-based composites tend to trigger pronounced initiation of coagulation without corresponding progression of clot formation. These findings emphasise the critical role of surface-engineered composite design in the development of safe, predictable, and effective haemostatic materials for CBRNE-related applications.

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ISOLATION OF *STREPTOMYCES* SP. FROM THE WOODED DUNES IN LATVIA AND THE CHARACTERISATION OF THEIR ANTIMICROBIAL POTENTIAL

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Background. The rise of antimicrobial resistance (AMR) has become a serious threat to global health. The predictions indicate that in 2050, bacterial infections will be responsible for nearly 2 million deaths annually, while antifungal resistance is predicted to cause more than 10 million deaths. The increased resistance against commonly used antimicrobials in the clinic required novel drug discovery and development. Actinobacteria, especially *Streptomyces* sp., are historically responsible for over 75% of known antimicrobials and remain a promising, yet underexplored, source of potentially new antibiotics. Currently, the focus of novel natural products discovery has shifted to unique and underexplored biotopes. Little to no bioprospecting in the Baltic region has been done before.

Aim. The aim of the study was to isolate new *Streptomyces* sp. strains from unique biotope in Latvia, wooded dunes, and characterise their antimicrobial potential in order to find novel antimicrobial natural products.

Methods. An underexplored biotopes — wooded dunes — was chosen for bioprospecting. Isolation of the strains was done by using dilution-to-extinction method on multiple different media. Isolates were cultivated in three diverse media to activate the production of more natural products, and multiple extracts were prepared. To determine the antimicrobial potential of the extracts, they were screened against a small panel of Gram+, Gram-, and fungal human pathogens, using broth dilution assays (BDAs).

Results. In total, 74 novel bacterial strains were isolated from the wooded dunes, out of which 23 strains belong to genus *Streptomyces* sp. The bioactivity screening revealed no activity against Gram-negative bacteria. Multiple extracts demonstrated activity against Gram-positive human pathogens, including *Staphylococcus aureus* and *Bacillus subtilis*. The bioactivity screening identified multiple candidates for the discovery of novel natural products.

Conclusion. This preliminary study has resulted in the selection of multiple strains with uncharacterised antimicrobial potential. Further studies are needed to characterise the chemical composition of the extracts, dereplicate and select the candidate strains for novel natural products discovery.

EFFECTS OF SILYMARIN, METFORMIN, AND PIOGLITAZONE ON LIPID ACCUMULATION AND OXIDATIVESTRESS IN A HEPG2 *IN VITRO* MODEL OF NON-ALCOHOLIC FATTY LIVER DISEASE

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Background. Non-alcoholic fatty liver disease (NAFLD) develops as a consequence of an imbalance between oxidative stress, inflammation, and hepatic lipid uptake, synthesis, and metabolism. Despite its high prevalence, there is currently no approved pharmacological therapy for NAFLD. Silymarin [1] and anti-diabetic drugs have been investigated in NAFLD patients because NAFLD and type 2 diabetes mellitus (T2DM) share common epidemiological and pathophysiological mechanisms. Cluster of differentiation 36 (CD36) plays a crucial role in hepatic steatosis by mediating fatty acid uptake, triglyceride storage, and secretion. However, the mechanisms by which CD36 inhibition may prevent NAFLD progression remain unclear, and no clinically approved CD36 inhibitors are available for NAFLD treatment.

Aim. This study aimed to evaluate the biological effects of silymarin, metformin, and pioglitazone in an *in vitro* NAFLD model using the human HepG2 cell line.

Methods. Human hepatocellular carcinoma HepG2 cells (ATCC HB-8065) were obtained from the American Type Culture Collection (ATCC, USA). Hepatic steatosis was induced by lipid overloading for 24 h using oleate: palmitate (2:1, 0.5 mM) complexed with 10% fatty acid-free bovine serum albumin (BSA). Lipid accumulation, lipid peroxidation, oxidative stress markers, inflammatory cytokines, CD36 level, cell viability, and albumin secretion were assessed using commercially available kits from Abcam, Thermo Fisher Scientific, Sigma-Aldrich and Merck. Fluorescence and absorbance were measured using an Infinite 200 PRO microplate reader ((Tecan Trading AG, Switzerland). Statistical analysis was performed using one-way ANOVA followed by Dunnett's multiple comparison test (GraphPad Prism 8.0; GraphPad Software, Inc., USA). All experiments were conducted in triplicate.

Results. Previous studies have suggested beneficial effects of silymarin supplementation in NAFLD; therefore, it was used as a reference compound. In the *in vitro* NAFLD model, all tested compounds significantly reduced fatty acid-induced increases in CD36 level, lipid accumulation, lipid peroxidation, and TNF-α secretion. None of the treatments restored the fatty acid-induced decrease in albumin secretion. Metformin and pioglitazone, which are not classical antioxidants, demonstrated lower antioxidant capacity compared with silymarin.

Conclusion. These findings support the hepatoprotective potential of anti-diabetic drugs and highlight their promise as therapeutic agents in NAFLD. CD36 remains a relevant novel molecular target warranting further investigation in the context of anti-diabetic drug action in NAFLD.

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VITAMIN D PATHWAY GENETICS AND NEDA OUTCOMES ACROSS MS THERAPIES IN A LATVIAN COHORT

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Background. Vitamin D signalling and transport are implicated in multiple sclerosis (MS) susceptibility and immune regulation. However, inter-individual variability in treatment response remains substantial, and genetic variation in the vitamin D pathway may contribute to therapy-dependent differences in achieving "no evidence of disease activity" (NEDA).

Aim. To evaluate whether polymorphisms in *VDR* and *GC* are associated with NEDA during the first two years after treatment initiation and to explore potential therapy- and interferon (IFN) preparation-specific effects.

Methods. Latvian MS patients were assessed for NEDA at years 1 and 2 after treatment initiation and stratified by therapy (IFN, GA, MX); IFN-treated patients were additionally stratified by IFN preparations (IFN-A, IFN-R, IFN-B/E). *VDR* (rs1544410, rs7975232, rs731236) and *GC* (rs7041, rs4588) variants were genotyped by PCR-based assays, and genotype distributions were compared by NEDA status within and between therapy groups. ORs were computed for NEDA- (OR < 1 protective; OR > 1 risk).

Results. Overall, vitamin D pathway loci showed therapy-dependent associations with NEDA, most prominently at year 2. Under IFN, *VDR* rs1544410 (G > A) was associated with NEDA ($P = 3.98\times10^{-2}$; V = 0.16), with AA+GA showing a more favourable NEDA profile compared with GG. A similar IFN-stratum association was observed for *VDR* rs731236 (T > C) ($P = 2.99\times10^{-2}$; V = 0.16). Within IFN-treated patients, stratification by IFN preparations further indicated preparation-specific heterogeneity for *VDR* rs7975232 (IFN-R: $P = 1.90\times10^{-2}$; V = 0.40) and *VDR* rs731236 (IFN-R: $P = 1.68\times10^{-2}$; V = 0.30). For vitamin D transport, *GC* rs4588 (C > A) differed between medication groups at year 2 ($P = 2.04\times10^{-2}$; V = 0.22) and showed opposite directions across therapies: AA+CA tended toward higher NEDA+ odds under IFN (OR ≈ 1.40) but lower NEDA+ odds under GA (OR ≈ 0.83), consistent with a potential gene–treatment interaction. In addition, *GC* rs7041 (G > T) showed a between-therapy difference in year 1 under MX ($P = 2.57\times10^{-2}$; V = 0.37), supporting therapy dependence also at earlier follow-up.

Conclusions. *VDR* and *GC* variants, especially *VDR* rs7975232/rs1544410/rs731236 and *GC* rs4588/rs7041, show therapy- and IFN preparation-specific associations with NEDA in this Latvian MS cohort, supporting a potential gene-treatment interaction. These findings should be validated in larger independent cohorts and incorporated into integrated prediction models combining genotype, clinical, and treatment variables.

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MANUFACTURING QUALITY ASSESSMENT OF SEMI-SOLID EXTRUSION 3D PRINTING FOR PHARMACEUTICAL FILMS: MICROSTRUCTURAL ANALYSIS AND USP COMPLIANCE EVALUATION

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Background. Pharmaceutical manufacturing requires stringent quality control to ensure dosage uniformity and therapeutic efficacy. United States Pharmacopeia General Chapter <905> mandates coefficient of variation below 6% for content uniformity, yet systematic quality assessments comparing 3D printing with conventional methods remain limited. Manufacturing precision directly impacts regulatory compliance and clinical translation potential.

Aim. To evaluate manufacturing consistency, microstructural characteristics, and USP <905> compliance of polyvinyl alcohol-based pharmaceutical films produced by

three methods: semi-solid extrusion 3D printing, solvent casting, and rotary electrospinning.

Methods. Pharmaceutical films containing menthol (5%), benzocaine (5%), and capsaicin (0–1%) were manufactured using 3D printing (n = 12 batches), solvent casting (n = 8 batches), and electrospinning (n = 13 batches) with matched formulations. Manufacturing precision was assessed through coefficient of variation analysis of mechanical properties per USP guidance. Scanning electron microscopy characterised surface morphology and internal architecture. Thickness uniformity and moisture content were determined per USP <731>. Statistical analysis included one-way ANOVA, Tukey's post-hoc test, and Cohen's d effect size calculations.

Results. Electrospinning demonstrated superior mechanical precision (CV: 13.36%), followed by 3D printing (CV: 21.29%) and casting (CV: 42.63%; $F(2,13) = 3.869$, $p = 0.048$). Three-dimensional printing achieved best thickness uniformity (CV: 7.3% versus 19.7% for casting, 2.7-fold improvement). Scanning electron microscopy revealed distinct microstructures correlating with manufacturing precision: casting exhibited severe surface roughness and extensive internal porosity from menthol volatility; 3D printing demonstrated smooth external surfaces with controlled internal architecture; electrospinning produced characteristic nanofibrous layered structure (film thickness 398 μm). Formulation optimisation with capsaicin achieved USP-compliant precision (CV: 4.39%) representing significant improvement over unoptimised formulation (CV: 51.86%; $p < 0.001$). Moisture analysis revealed electrospinning optimal control (5.6%) versus 3D printing elevated retention (13.5%, 2.4-fold difference). Only two conditions achieved USP <905> compliance (CV < 6%): 3D printing with capsaicin and electrospinning at optimised volume.

Conclusions. Manufacturing method significantly impacts pharmaceutical film quality attributes. Electrospinning provides superior mechanical consistency ideal for applications requiring uniform drug distribution. Three-dimensional printing offers exceptional dimensional control and achieves regulatory compliance through formulation optimisation. Scanning electron microscopy confirms direct correlation between surface microstructure and manufacturing precision. Method selection should be based on critical quality attributes prioritised for specific pharmaceutical applications. The capsaicin stabilization phenomenon warrants mechanistic investigation for broader formulation applications.

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SEMI-SOLID EXTRUSION 3D PRINTING ENHANCES TRANSDERMAL MENTHOL DELIVERY: A COMPARATIVE MANUFACTURING STUDY

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Background. Three-dimensional printing enables precise control of pharmaceutical dosage forms, but systematic comparisons with conventional manufacturing for transdermal delivery are lacking. Polyvinyl alcohol-based films offer biocompatibility and controlled drug release, making them ideal candidates for topical analgesic applications.

Aim. This proof-of-concept study evaluated whether semi-solid extrusion 3D printing enhances transdermal menthol delivery compared to conventional solvent casting methods.

Methods. Polyvinyl alcohol-based films containing menthol (5% w/w) were prepared by 3D printing (n = 12), solvent casting (n = 12), and robotic spraying (n =3, exploratory) with matched formulations for primary comparison. *Ex vivo* permeation studies used human abdominal skin (Caucasian females, 30–55 years, n = 10 donors) in flow-through diffusion cells over 24 hours. Tissue menthol concentrations were determined using validated LC-MS/MS methodology. Manufacturing precision was assessed through thickness uniformity, drug content uniformity, and moisture content measurements.

Results. 3D-printed films achieved 4.4-fold higher epidermal menthol accumulation versus casting (22.0 ± 3.8 μg/ml vs 5.0 ± 0.8 μg/ml; $p = 0.0004$; Cohen's d = 1.79), creating a therapeutic drug reservoir ideal for localised pain relief. Both methods showed comparable dermal penetration (95.6 ± 5.0 μg/cm² vs 76.1 ± 8.0 μg/cm²; 1.26-fold; $p = 0.048$). 3D printing demonstrated superior manufacturing precision with thickness coefficient of variation 7.3% versus 19.7% for casting, controlled moisture content (12.4 ± 0.3%), and favourable drug content uniformity (RSD 4.7% vs 9.5%). Time-course analysis revealed sustained menthol accumulation over 24 hours with immediate drug release and no lag phase.

Conclusions. Semi-solid extrusion 3D printing establishes a promising platform for topical analgesic delivery with 4.4-fold epidermal enhancement, creating a therapeutic drug reservoir while maintaining transdermal penetration. Superior manufacturing precision and controlled release kinetics support clinical translation potential. Critical next steps include multi-analyte validation, microstructural characterisation, and diverse donor studies.

Acknowledgements. The authors declare no conflicts of interest. This research received no specific funding from public, commercial, or not-for-profit sectors.

NEUROPROTECTIVE POTENTIAL OF NATURAL COMPOUNDS IN *IN VITRO* MODELS OF PARKINSON'S DISEASE

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Background. Parkinson's disease (PD) is a neurodegenerative disorder characterised by progressive loss of dopaminergic (DA) neurons and the accumulation of Lewy bodies in the brain, which are mainly composed of α-synuclein (αSyn). Dysregulation of αSyn homeostasis and impairment of protein degradation pathways are key contributors to PD pathogenesis. Elevated αSyn levels have been shown to impair 20S proteasome function in biochemical and cellular models. In parallel, monoamine oxidase B (MAO-B) plays a critical role in DA catabolism; thus, MAO-B inhibition increases synaptic DA levels and enhances dopaminergic signalling. Advances in understanding the molecular mechanisms underlying PD have stimulated interest in identifying natural compounds capable of slowing or halting neurodegeneration.

Aim. The aim of this study was to evaluate the anti-Parkinsonian effects of selected polyphenols in *in vitro* PD models focusing on DA metabolism and αSyn aggregation.

Methods. The polyphenols oregonin, apigenin, curcumin, and betulin were investigated alongside reference compounds — the MAO-B inhibitor pargyline and the 20S proteasome inhibitor epoxomicin. MAO activity was assessed using the MAK136 assay kit. αSyn aggregation was evaluated by a thioflavin T (ThT) fluorescence assay [1]. 20S proteasome activity was measured using the Proteasome Activity Kit (BML-AK740). All reagents were obtained from Sigma-Aldrich (USA) or Enzo Life Sciences via AH Diagnostics (Denmark). Fluorescence and absorbance were measured with an Infinite 200 PRO plate reader (Tecan Trading AG, Switzerland). Statistical analysis was performed using one-way ANOVA followed by Dunnett's multiple comparison test (Graph- Pad Prism, Version 8.0; GraphPad Software, Inc., USA). All experiments were conducted in triplicate.

Results. All tested polyphenols inhibited MAO-B activity at concentrations ranging from 1 to 100 μM. Curcumin slightly enhanced chymotrypsin-like activity of the 20S proteasome at low concentrations (0.1–10 μM) but inhibited proteasome activity at 100 μM. Betulin had no significant effect on 20S proteasome activity, whereas apigenin and oregonin acted as inhibitors. All polyphenols significantly reduced αSyn aggregation *in vitro* after four days of incubation at 37 ^{o}C.

Conclusion. The data indicate that oregonin, apigenin, curcumin, and betulin act as multifunctional agents targeting key neurodegenerative processes in PD by inhibiting MAO-B activity and suppressing toxic αSyn ag- gregation. The role of 20S proteasome modulation in neuroprotection requires further investigation. Overall, these findings support the neuroprotective potential of polyphenols and highlight their promise as adjuvant agents in PD therapy.

Acknowledgement. The authors declare no conflicts of interest. This study was supported by the University of Latvia basic grant Y5-AZ114-ZF-N-840.

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THERAPY-SPECIFIC ASSOCIATIONS OF PROTEASOME GENE POLYMORPHISMS WITH NEDA STATUS IN A LATVIAN MULTIPLE SCLEROSIS COHORT

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Background. Achieving "no evidence of disease activity" (NEDA) is a clinically relevant treatment target in multiple sclerosis (MS), yet NEDA rates vary across therapies and individuals. Genetic variation in proteasome-related genes may influence immune pathways and contribute to therapy-dependent differences in disease activity control.

Aim. To test whether selected proteasome-gene polymorphisms are associated with NEDA during the first two years after treatment initiation and to explore therapy-specific genotype effects across interferon (IFN), glatiramer acetate (GA), and mitoxantrone (MX) groups.

Methods. MS patients from a Latvian cohort were evaluated for NEDA in year 1 and year 2 after treatment initiation and stratified by therapy (IFN, GA, MX). SNPs in proteasome-related genes (*PSMB5* rs11543947; *PSMA6* rs2277460 and rs1048990; *PSMA3* rs2348071; *PSMC6* rs2295826/rs2295827) were genotyped using PCR-based assays. Genotype distributions were compared by NEDA status within and between therapy groups. ORs were computed for NEDA–; OR < 1 indicates a protective association and OR > 1 increased risk. Effect sizes are reported as Cramér's V.

Results. The strongest therapy-dependent association over two years was observed for *PSMC6* rs2295826/rs2295827. The combined genotype group (GG/TT+AG/CT) differed between medication groups ($P = 2.20\times10^{-3}$; V = 0.37). In IFN-treated patients, GG/TT + AG/CT showed a more favourable NEDA profile (NEDA+ 67.69%) and reduced odds of NEDA-negativity ($P = 2.48\times10^{-3}$; OR = 0.38). In contrast, in GA-treated patients the same genotype group was associated with low NEDA+ (16.67%) and increased odds of NEDA-negativity ($P = 4.22\times10^{-2}$; OR = 5.67).

Within IFN-treated patients, differences across IFN preparations were observed for *PSMA6* rs1048990 after one year (GG+CG distribution across IFN-A/IFN-R/IFN-B/E: $P = 2.80\times10^{-2}$; V = 0.45). In IFN-A, GG+CG was linked to higher odds of NEDA-negativity ($P = 8.44\times10^{-3}$; OR = 16.29). In year 2, an association was also observed for IFN-B/E ($P = 4.31\times10^{-2}$; OR = 4.24). After two years, *PSMA6* rs2277460 also differed across IFN preparations (CA genotype: $P = 4.55\times10^{-2}$; V = 0.49); in IFN-B/E, CA carriers were predominantly NEDA– (83.33%; $P = 3.29\times10^{-2}$; OR = 5.14).

Conclusions. Proteasome-related variants, particularly *PSMC6* rs2295826/rs2295827 and *PSMA6* polymorphisms, show therapy-specific associations with NEDA, consistent with gene–treatment interaction. Notably, *PSMC6* (GG/TT+AG/CT) showed opposite directions across therapies (more favourable under IFN, less favourable under GA). These loci warrant validation in larger independent cohorts.

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EXPLORATION OF COCRYSTAL FORMATION BETWEEN NITROFURAN ANTIBIOTICS AND UREA DERIVATIVES

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Background. Cocrystallisation is a well-established solid-state strategy for improving the pharmaceutical performance of active pharmaceutical ingredients (APIs), particularly in terms of solubility, stability, and manufacturability [1–3]. Pharmaceutical cocrystals are composed of an API and a pharmaceutically acceptable, non-ionised coformer arranged within a single crystalline phase. This approach enables modification of API properties without altering the molecular structure or pharmacological activity. In this study, two structurally related nitrofuran antibiotics, nitrofurantoin (NF) and furazidin (FUR), were selected as model APIs due to their limited solubility and known solid-state

variability. NF is known to form a cocrystal with urea [4], making this system suitable for evaluating coformer selection strategies.

Aim. The aim of this study was to assess whether structurally similar APIs, NF and FUR, exhibit comparable cocrystal-forming behaviour with a series of pharmaceutically relevant urea derivatives, and to evaluate the implications of these findings for rational coformer selection in pharmaceutical cocrystal design.

Methods. Cocrystal screening was carried out by liquid-assisted grinding (LAG) using acetonitrile. APIs and coformers were tested in 1:1, 1:2, and 2:1 stoichiometric ratios. The obtained solids were analysed by powder X-ray diffraction (PXRD). When new crystalline phases were detected, single crystals were grown from acetonitrile solution and characterised by single-crystal X-ray diffraction (SCXRD).

Results. Nine urea derivatives were evaluated as potential coformers, resulting in the formation of seven new crystalline phases, including four cocrystals with FUR and three with NF. While urea formed cocrystals with both APIs, substitution of the urea scaffold significantly influenced cocrystallisation outcomes. Structural features of FUR, particularly the extended C–C linkage between heterocycles, enabled cocrystal formation with urea derivatives capable of additional aromatic interactions. Minor substitution at one nitrogen atom of urea allowed cocrystal formation with both APIs; however, larger substituents restricted cocrystal formation to NF only. Despite employing similar hydrogen-bonding motifs, variations in coformer structure led to distinct solid-state outcomes, highlighting the sensitivity of cocrystal formation to subtle molecular changes.

Conclusions. Although NF and FUR share close structural similarity, small molecular differences substantially affect their cocrystal-forming behaviour. These findings demonstrate that structural analogy alone is insufficient for predicting pharmaceutical cocrystal formation and underscore the importance of empirical screening during solid-form development. The results provide valuable insight for rational coformer selection and solid-state optimisation of APIs with challenging physicochemical properties.

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ADVERSE EFFECTS OF BIOLOGICAL THERAPIES WITH ADALIMUMAB, USTEKINUMAB, SECUKINUMAB, AND RISANKIZUMAB IN MODERATE-TO-SEVERE PSORIASIS VULGARIS

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Background. Management of moderate-to-severe psoriasis remains challenging. Introduction of newer biological therapies has significantly improved disease control. However, their safety profiles and laboratory-defined adverse effects in routine clinical practice require further evaluation.

Aim. The aim of this study was to evaluate treatment outcomes of biological therapies in patients with moderate-to-severe psoriasis in routine clinical practice, focusing on treatment response, therapy switching, prior biologic exposure, and laboratory-defined adverse effects, including elevated alanine aminotransferase (ALT) and/or gamma-glutamyl transferase (GGT), reduced estimated glomerular filtration rate (eGFR) and neutropenia.

Methods. A retrospective study (2019–2025) included 23 adult patients with moderate-to-severe psoriasis treated at Ventspils Poliklīnika with adalimumab, ustekinumab, secukinumab, or risankizumab. Inclusion criteria were a baseline PASI > 10 and PGA score of 3–4. We compared the occurrence of ALT and/or GGT, reduced eGFR and neutropenia. Outcomes were evaluated using patient-years of exposure, and adverse events were expressed as incidence rates.

Results. Eight patients were biologic-naïve, while seven had previously received secukinumab. Latent tuberculosis was identified in eight patients, all of whom received concomitant isoniazid therapy according to local guidelines.

Among biologic-naïve patients treated with adalimumab, 30% required switching due to failure to achieve PASI 50. Overall, seven patients required switching between biologic agents (ustekinumab, secukinumab or risankizumab) because of inadequate response to adalimumab.

During 45.34 patient-years of adalimumab exposure, the incidence rate of elevated liver enzymes (ALT and/or GGT) was 0.397. A reduction in estimated glomerular filtration rate to < 90 ml/min/1.73 m² was observed with an incidence rate of 0.331. A decrease in absolute neutrophil count below 1.92×10^9/l occurred with an incidence rate of 0.154 during adalimumab therapy.

Among two patients switched from adalimumab to secukinumab, no reduction in estimated glomerular filtration rate was observed during adalimumab treatment (incidence rate 0). During 7.42 patient-years of secukinumab exposure, a reduction in estimated GFR to < 90 ml/min/1.73 m² was observed with an incidence rate of 0.539.

Conclusion. We conclude that, according to the European Medicines Agency (EMA) frequency classification, elevated liver enzymes, reduced glomerular filtration rate, and neutropenia associated with adalimumab are classified as uncommon adverse effects.

In two patients switched from adalimumab to secukinumab, estimated glomerular filtration rate deteriorated from previously normal values.

Latent tuberculosis is not a contraindication to biological therapy when appropriate preventive treatment is provided.

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