Book of Poster Abstracts

1st Annual Conference of the NETPHARM project

Hradec Králové, Czech Republic

14th-15th 2025

Co-funded by the European Union

MINISTRY OF EDUCATION, YOUTH AND SPORTS

NETPHARM

IMPORTANT ADDRESSES

1_Conference venue
Hotel Nové Adalbertinum
https://noveadalbertinum.cz/en
Velké nám. 32, 500 03 Hradec Králové
https://maps.app.goo.gl/jetSq92DEHzrF2sMA

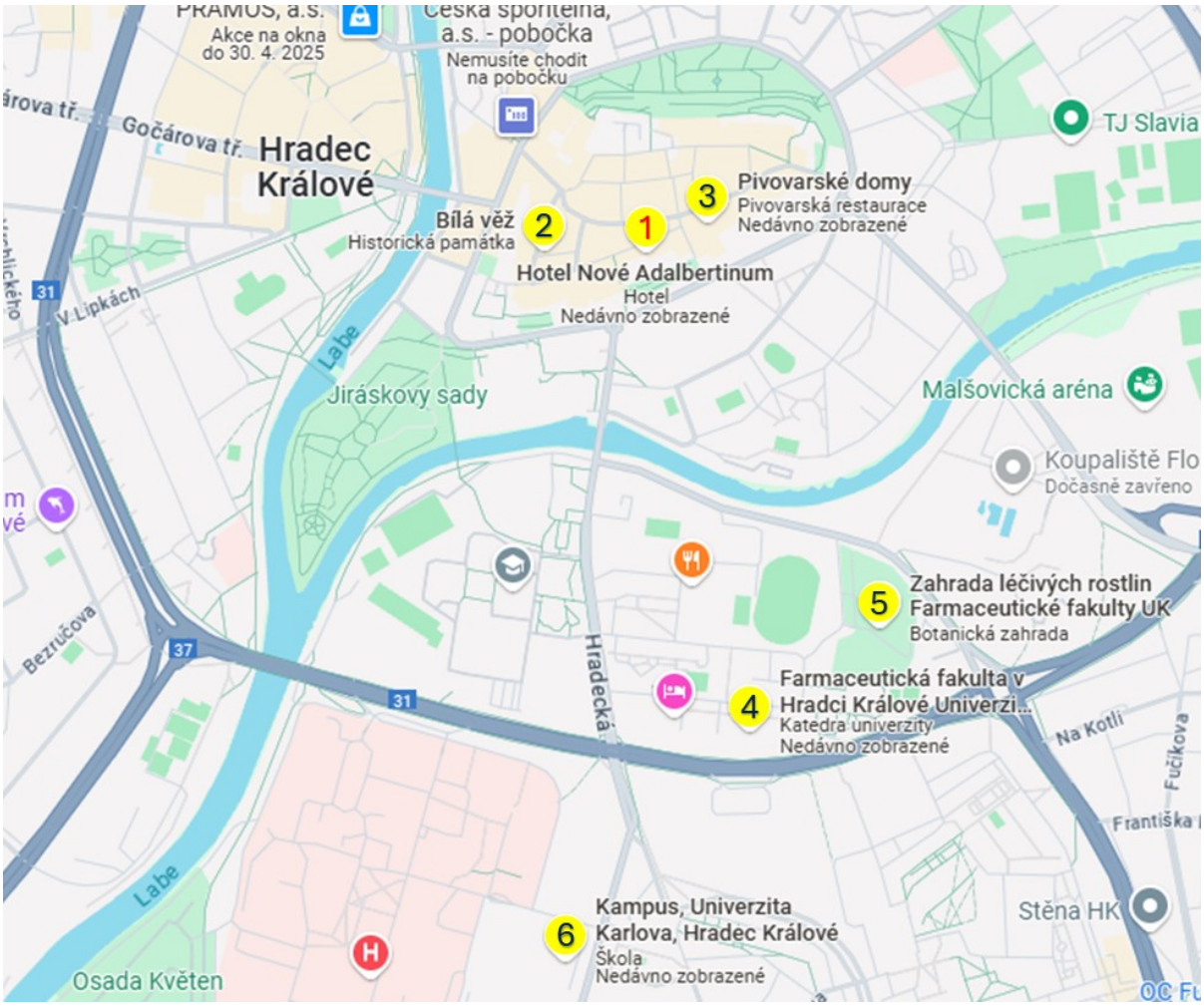
2_White Tower – Guided tour (at your own expense)
Velké nám. 87/2, 500 03 Hradec Králové 3
https://maps.app.goo.gl/8pA26NCoUSU9JsEeA

3_ISAB Networking dinner – Pivovarské domy
https://www.pivovarskedomy.cz/pivnice/
Velké nám. 26, 500 03 Hradec Králové 3
https://maps.app.goo.gl/46Ejx33qu5v1ZP417

4_Charles University, Faculty Of Pharmacy
Akademika Heyrovského 1203/8, 500 03 Hradec Králové
Charles University, Faculty of Pharmacy
https://maps.app.goo.gl/bDR9z78o6nk5th389

5_Garden of medicinal plants (CU, FoP)
Botanická, 500 05 Hradec Králové 3
Garden of Medicinal Plants | Charles University, Faculty of Pharmacy
https://maps.app.goo.gl/7AV1GR6iKL8aUYr87

6_ Campus of Charles University in Hradec Králové
Zborovská 2089, 500 03 Hradec Králové
Campus of Charles University in Hradec Králové | MEPHARED
https://maps.app.goo.gl/G4zdd1eFSS2Tm5Gq6



NETPHARM
New Technologies for Translational Research in Pharmaceutical Sciences

WELCOME MESSAGE

Dear Participants,

On behalf of the organizing committee, we warmly welcome you to the 1st Annual Conference of the NETPHARM project, hosted by the Faculty of Pharmacy in Hradec Králové, Charles University.

The conference brings together researchers from all institutions participating in the New Technologies for Translational Research in Pharmaceutical Sciences (NETPHARM) project. It is a great opportunity for us to present our latest scientific work and exchange insights on diverse topics, ranging from organic synthesis and medicinal chemistry to pharmaceutical technology, pharmacology, biochemistry, and clinical pharmacy. A key feature of this conference is its support of our PhD students and junior scientists. We are proud to provide these young scientists with a platform to share their scientific results with their more experienced colleagues in the poster session.

In addition to the rich scientific content, the NETPHARM conference provides an excellent opportunity for networking, discussions, forming new collaborations, and strengthening both professional and personal relationships. Finally, the conference is a nice opportunity to visit the Faculty of Pharmacy, Charles University, and Hradec Králové, the city known as the Salon of the Republic, featuring many examples of modernist architecture.

We look forward to a productive conference and engaging discussions.

Sincerely,

Petr Pavek

ABOUT THE NETPHARM PROJECT

NETPHARM – New Technologies for Translational Research in Pharmaceutical Sciences

The NETPHARM project aims to establish a dynamic, interdisciplinary network of leading Czech research institutions focused on the translational development of advanced therapies and drug delivery systems. By combining expertise in pharmaceutical chemistry, pharmacology, drug formulation, clinical pharmacy, and in silico/in vitro methodologies, NETPHARM fosters innovation in the development of (nano)formulations and therapeutic strategies tailored to vulnerable patient subpopulations.

The consortium integrates academic excellence from Charles University (Faculties of Pharmacy and Medicine in Hradec Králové), the University of Chemistry and Technology in Prague, Masaryk University (CEITEC), and the Czech Academy of Sciences (IOCB and IMC). NETPHARM's five thematic work packages focus on key areas ranging from novel diagnostic probes and therapeutic molecules, through targeted nanoformulations, to clinical decision tools and AI-based modeling.

Supported by the Ministry of Education, Youth and Sports of the Czech Republic and co-funded by the EU, the project is set to strengthen research infrastructure, foster international collaborations, and boost publication and patent output. NETPHARM brings together over 170 researchers and engages a strong international advisory board to enhance global competitiveness and support long-term impacts in science and clinical practice.

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P01

New selective PXR antagonist and its effects in the humanized mouse model

Klára Dohnalová [1,2], Martin Ambrož [3], Rajamanikkam Kamaraj [3], Radim Nencka [4], Petr Pávek [3]

[1] Czech Centre for Phenogenomics, Institute of Molecular Genetics of the Czech Academy of Sciences, Vídeňská 1083, 142 20, Prague, Czech Republic

[2] First Faculty of Medicine, Charles University, Kateřinská 32, 112 08, Prague, Czech Republic

[3] Department of Pharmacology and Toxicology, Faculty of Pharmacy in Hradec Králové, Charles University, Akademika Heyrovského 1203, 500 05, Hradec Králové, Czech Republic

[4] Institute of Organic Chemistry and Biochemistry, Czech Academy of Sciences, Flemingovo náměstí 2, 166 10, Prague 6, Czech Republic

ABSTRACT

Objectives: Pregnane X receptor (PXR) is a ligand-activated transcription factor that plays a crucial role in the metabolism of both xenobiotics and endobiotics. Its importance in xenobiotic metabolism is well-documented, and it is a key player in many drug-drug interactions. Another significant aspect of PXR regulation is its role in endogenous metabolism. PXR can modulate the metabolism of lipids, glucose, cholesterol, and bile acids. Activation of PXR in the liver is one of the factors linked to liver steatosis. PXR antagonists could potentially offer therapeutic benefits for this condition, but to date, only a limited number of PXR antagonists have been identified. Common issues with known PXR antagonists include weak efficacy, low specificity, and toxicity.

Methods: In our *in vitro* screening, we tested a series of potential antagonists, identifying MI-891 as a promising candidate. Subsequent *in vivo* studies were conducted using an HFD-fed CAR-PXR-CYP3A4/3A7-humanized mouse model.

Results: Our compound was able to reduce triglyceride production in liver tissue. Lipidomic analysis showed its effect was primarily on shorter and more saturated lipids. To further investigate the mechanism of action, we performed RT-qPCR, focusing on genes associated with triacylglycerols and fatty acids. Shifts in gene expression were further examined at the protein level via Western blot.

Conclusion: In conclusion, our findings demonstrate that MI-891 inhibits PXR activation in the mouse model, leading to the downregulation of transcription and translation, as well as reduced lipid production in the liver.

The project New Technologies for Translational Research in Pharmaceutical Sciences /NETPHARM, project ID CZ.02.01.01/00/22_008/0004607, is co-funded by the European Union.

P02

Investigation of the Functional Roles of MDR-Associated ABC Transporters in Ex Vivo Lung Tumor Primary Culture

BUDAGAGA, Y.[1], HANKE, I.[2], ROZKOŠ T.[3], Hofman, J.[1]

[1] Department of Pharmacology and Toxicology, Faculty of Pharmacy in Hradec Králové, Charles University, Czech Republic

[2] Department of Cardiac Surgery, Faculty of Medicine, Charles University and University Hospital in Hradec Králové, Sokolská 581, 500 05 Hradec Králové, Czech Republic

[3] The Fingerland Department of Pathology, Faculty of Medicine, Charles University and University Hospital in Hradec Králové, Czech Republic, Sokolská 581, 500 05 Hradec Králové, Czech Republic

ABSTRACT

Objectives

Lung cancer is the second leading cause of cancer-related deaths in both genders. Multidrug resistance (MDR) significantly limits the effectiveness of anticancer therapies, often due to drug efflux via ATP-binding cassette (ABC) transporters. While some studies have examined ABC transporter expression in lung cancer, their functional roles in MDR are not well understood. This study aims to develop a protocol for patient-derived non-small cell lung cancer (NSCLC) explants and assess the expression and activity of ABCB1, ABCG2, and ABCC1 transporters.

Methods

Sixteen primary NSCLC cultures were generated from biopsies collected post-lobectomy. Western blot analysis identified varying expression levels of ABCB1, ABCG2, and ABCC1 transporters among patients. The functional activity was assessed using flow cytometry-based accumulation assays with doxorubicin and mitoxantrone as fluorescent substrates. To evaluate the impact of transporter inhibition, specific inhibitors (LY335979 for ABCB1, Ko143 for ABCG2, and MK-571 for ABCC1) were applied as positive controls.

Results

The expression levels of ABC transporters varied significantly among patient-derived NSCLC explants. Flow cytometric accumulation studies demonstrated an association between transporter expression levels and drug accumulation. However, model inhibitors caused insignificant changes in the accumulation of model cytostatic substrates and vice versa.

Conclusion

This study provides evidence that ABCB1, ABCG2, and ABCC1 transporters may play a role in MDR against conventional chemotherapeutics in NSCLC patients. The established explant model serves as a valuable tool for further investigations into drug resistance mechanisms and potential therapeutic strategies targeting ABC transporters in lung cancer.

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P03

IMPACT OF MASLD ON THE DETOXIFICATION SYSTEM IN AN *IN VIVO* MODEL

Horní, M.[1], Svobodová, G.[1], Velecká, E.[1], Maletínská, L.[2], Boušová, I.[1]

[1] Department of Biochemical Sciences, Faculty of Pharmacy in Hradec Králové, Charles University, Czech Republic

[2] Department of Biochemical Sciences, Faculty of Pharmacy in Hradec Králové, Charles University, Czech Republic

ABSTRACT

Objectives: The liver plays a major role in detoxifying both endogenous and exogenous substances. Metabolic dysfunction-associated steatotic liver disease (MASLD), a chronic liver disease characterized by excessive production of reactive oxygen species, can modulate detoxification pathways and thus interfere with drug metabolism and antioxidant protection of the organism. This study aimed to determine how MASLD progression impacts the expression and activity of selected detoxification enzymes inc. superoxide dismutase (SOD), NAD(P)H:quinone oxidoreductase 1 (NQO1), and carbonyl reductase 1 (CBR1) in the mouse liver.

Methods: The C57BL/6N male mice were divided into two groups, one fed a standard diet (STD) and the other a high fat, fructose, and cholesterol (FFC) diet from the age of 8 weeks for 1-6 months. The liver samples from both groups were collected at seven 4-week intervals. The mRNA expression was determined using RT-qPCR method, protein expression was evaluated using western blotting with chemiluminescent detection, and enzymatic activities were assessed spectrophotometrically using the appropriate substrates.

Results: Feeding the FFC diet led to alterations in gene and/or protein expression of certain observed enzymes and increased activity of all observed enzymes, mainly in the latter time intervals, compared to age-matched STD-fed mice.

Conclusion: This study not only shows the effect of the FFC diet on the expression and activity of detoxification enzymes but also reveals the changes in their expression and activity during MASLD progression.

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P04

THE EFFECT OF 4 -METHYLCATECHOL IN GERIATRIC PATIENTS

Marcel Hrubša [1], Přemysl Mladěnka [1]

[1] Department of Pharmacology and Toxicology

ABSTRACT

Objectives: 1) to explore the differences between platelet aggregation in healthy adults and geriatric patients with polypharmacy, 2) to investigate if 4-methylcatechol, a metabolite of food flavonoids, cannot serve as a suitable novel antiplaletet drug

Methods: Whole blood aggregometry with various aggregation inducers and standard drugs was utilized. Acetylsalicylic acid was used as a standard in arachidonic acid and collagen induced blood aggregation.

Results: There were significant differences in response to collagen and ristocetin and the effect of acetylsalicylic acid and 4–methylcatechol was also different between the healthy volunteers and elderly patients.

Conclusion: Polypharmacy and related increased risk of drug interactions and side effects are very common in elderly patients. Geriatric patients also react differently to commonly used drugs and platelet aggregation inducers and hence have altered haemostasis and drug response. 4– methylcatechol is a potent antiplatelet compound which may provide an efficient alternative to currently used antiplatelet drugs with lower risk of drug interactions.

The project New Technologies for Translational Research in Pharmaceutical Sciences /NETPHARM, project ID CZ.02.01.01/00/22_008/0004607, is co-funded by the European Union.

P05

FLUBENDAZOLE AS A POTENTIAL THERAPEUTIC AGENT FOR A PANCREATIC DUCTAL ADENOCARCINOMA

Kohoutová E. [1], Skarková V. [2], Kápičková K. [2], Vítovcová B. [3], Rudolf E. [2], Matoušková P. [1]

[1] Department of Biochemical Sciences, Faculty of Pharmacy in Hradec Králové, Charles University

[2] Department of Medical Biology and Genetics, Faculty of Medicine in Hradec Králové, Charles University

[3] Department of Biology, Faculty of Medicine in Plzeň, Charles University

ABSTRACT

Objectives: Pancreatic ductal adenocarcinoma (PDAC) is a highly aggressive malignancy with a poor prognosis, with only 5–10% of patients surviving beyond five years post-diagnosis. Current treatment strategies remain largely ineffective, necessitating the identification of novel therapeutic agents. Flubendazole (FLU), a benzimidazole anthelmintic, has demonstrated significant antitumor activity by inhibiting microtubule polymerization in various cancers. This study aims to evaluate the therapeutic potential of FLU in PDAC cells and to explore its effects on cell viability, proliferation, and apoptosis.

Methods: Stabilized PDAC cell lines (BxPC-3, PANC-1, MIA-PaCa-2, Patu-8902) were utilized to assess FLU efficacy. Cell viability was determined using the WST-1 assay for 2D cultures and the CellTiter-Glo® 3D assay for 3D cultures derived from the BxPC-3 cell line and prepared with Geltrex. Morphological changes were analyzed via phase-contrast and fluorescence microscopy. Gene and protein expression variations were examined through qPCR and western blotting.

Results: FLU significantly reduced PDAC cell proliferation and induced apoptosis in a dose-dependent manner. Morphological alterations were observed in all treated cell lines, with 3D cultures displaying changes at higher FLU concentrations compared to 2D cultures. Differences in gene and protein expression associated with microtubule dynamics and apoptotic pathways were evident across cell lines, supporting FLU's role as a microtubule inhibitor.

Conclusion: Our findings demonstrate that FLU exerts potent antitumor effects on PDAC cells by disrupting microtubule function and inducing apoptosis. These results highlight FLU as a promising candidate for further investigation in PDAC treatment and support its potential integration into novel therapeutic strategies targeting this devastating disease.

The project New Technologies for Translational Research in Pharmaceutical Sciences /NETPHARM, project ID CZ.02.01.01/00/22_008/0004607, is co-funded by the European Union.

P06

Nematocidal activity of new benzhydroxamic acid derivatives in *Caenorhabditis elegans*

Karolína Štěrbová [1], Lenka Skálová [1], Petra Matoušková [1]

[1] Department of Biochemical Sciences, Faculty of Pharmacy, Charles University, Hradec Králové, Czech Republic

ABSTRACT

Objectives: Parasitic nematodes are responsible for a wide range of diseases in animals and humans. Although anthelmintics are commonly used for treatment, their effectiveness is declining due to the increasing prevalence of resistance in nematode populations.

In our recent study, 13 novel derivatives of benzhydroxamic acid (OMKs) were developed and their potential anthelmintic activity was tested on the parasitic nematode *Haemonchus contortus* (barber's pole worm). Among these compounds, OMK207 and OMK211 demonstrated reductions in the viability and motility of larval and adult stages of both drug-sensitive (ISE) and drug-resistant (IRE) strains of *H. contortus*.

Even though, *H. contortus* is a suitable candidate for this study, working with parasitic nematodes requires a specific approach that often makes quantitative experiments in their natural habitat difficult. Therefore, this work aims to incorporate an additional model organism, the free-living nematode *Caenorhabditis elegans*, to support our future research.

Methods: To optimize the larval development assay (LDA) and motility assay, the well-known anthelmintics albendazole (ABZ) and ivermectin (IVM) were used. Drug sensitivity was assessed by exposing a synchronized L1 population of wild-type *C. elegans* strain N2 Bristol (N2B) and ivermectin-resistant strain (IVR10) to varying doses of ABZ, IVM, or OMKs. After 55h on agar or 74 h in S. medium, adults were counted microscopically. The effect of ABZ on movement inhibition was evaluated using WormMicroTracker.

Results: The results indicate that increasing concentrations of albendazole lead to pronounced morphological effects, including a curled body posture, reduced adult size, and inhibited movement. The motility of adult nematodes decreased by 50% at 1.5 µM ABZ, with complete inhibition observed at 100 µM. LDA results with ivermectin confirmed a diversity in sensitivity between the two strains. OMK207 and OMK211 inhibited *C. elegans* development with IC_{50} values of 13 µM and 23 µM, respectively.

Conclusion: Our study of novel anthelmintic development was extended to include *C. elegans* as an additional model organism. The LDA and motility assay methodologies were also introduced to monitor the anthelmintic activity of new compounds. Furthermore, the inhibitory effects of OMK207 and OMK211 on *C. elegans* development were confirmed, supporting their potential as promising novel compounds with anthelmintic activity.

The project New Technologies for Translational Research in Pharmaceutical Sciences /NETPHARM, project ID CZ.02.01.01/00/22_008/0004607, is co-funded by the European Union.

P07

Dendralenes as linkers in bioconjugation chemistry

Bartoloměj Grobař [1], Petr Matouš [1], Milan Pour [1]

[1] Department of organic and bioorganic chemistry, Faculty of Pharmacy in Hradec Králové, Charles university

ABSTRACT

Objectives: Utilizing Stille coupling, our group developed a method that leads to variously derived dendralenes. Our current goal is to use this method to get water-soluble, electron rich dendralenes. These molecules can undergo Diels-Alder reaction in click-like fashion and can therefore be used as linkers in bioconjugation chemistry. The final product will be an antibody with two anthracycline antibiotic molecules attached via dendralene linker.

Methods: The key step of the synthesis involves Stille coupling. The material is analyzed using primarily NMR spectroscopy and mass spectroscopy. The studies of reactivity were monitored via HPLC.

Results: So far, we have been able to make one potential linker candidate that reacts with maleimides in click-like fashion, however only at high concentrations. Currently attempts to make some more reactive yet stable candidates are being carried out.

Conclusion: We have discovered that dendralenes can undergo Diels-Alder reaction in click-like fashion. Our search for an ideal linker candidate is still ongoing due to unsatisfactory reactivity or stability of our current compounds.

The project New Technologies for Translational Research in Pharmaceutical Sciences /NETPHARM, project ID CZ.02.01.01/00/22_008/0004607, is co-funded by the European Union.

P08

A BIOMIMETIC CONVERGENT TOTAL SYNTHESIS OF PRUNOLACTONE A

Michal Kadaník [1], Ekaterina Frantsuzova [1], Petr Matouš [1], Lucie Nováková [1], Jiří Kuneš [1], Manola Bonsignore [2], Erik Andris [2], Zdeňka Růžičková [3], Milan Pour [1]

[1] Faculty of Pharmacy, Charles University, Heyrovského 1203, 500 05 Hradec Králové, Czech Republic
[2] Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, Flemingovo náměstí 2, 166 10 Prague 6, Czech Republic
[3] Faculty of Chemical Technology, University of Pardubice, Studentská 573, 532 10 Pardubice, Czech Republic

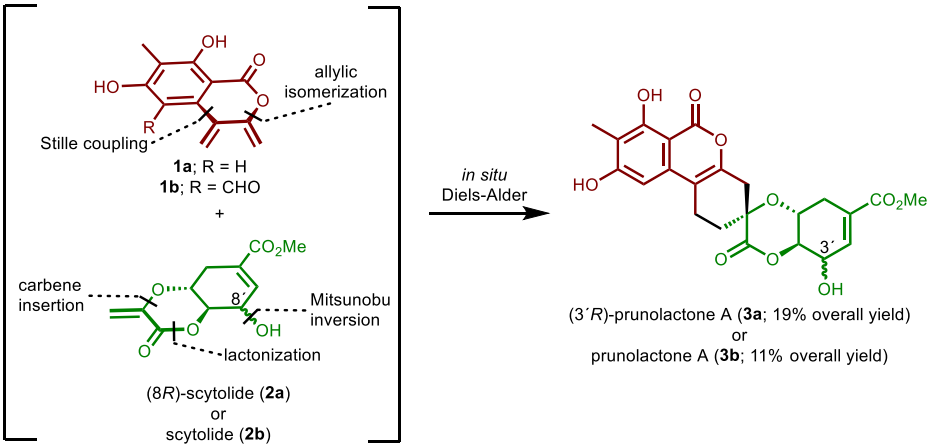
ABSTRACT

Objectives: Prunolactones A–G represent a novel group of isocoumarin derivatives possessing an unprecedented 6/6/6/6/6 spiropentacyclic skeleton and interesting proangiogenic activity. Biosynthetically, they were proposed to arise *via* the key Diels-Alder reaction of scytolide (**2b**; Scheme 1), formed by the shikimate pathway, and 3,4-bis(methylene)isocoumarin intermediate **1**, derived from the polyketide pathway. In this study, we report the first approach toward prunolactone A (**3b**), resulting in 10-step synthesis, including a crucial biomimetic cycloaddition of *in situ* generated diene **1a** and scytolide (**2b**).

Methods: The reactions were carried out in oven-dried glassware using Schlenk line techniques with magnetic stirring and dried solvents under Ar atmosphere.

Results: While the precursor of diene was easily prepared from commercially available 1,3-dimethoxytoluene, the synthesis of scytolide (**2b**) appeared to be more challenging. Although the preparation of this dienophile is known in the literature, the final reaction step provides an inseparable mixture of two epimers – scytolide (**2b**) and (8*R*)-scytolide (**2a**) in the molar ratio of 5 : 1, which can lead to the formation of undesired stereoisomers of prunolactone A (**3b**) in the *in situ* Diels-Alder reaction. Therefore, a new methodology based on Mitsunobu inversion was developed, yielding the scytolide (**2b**) in stereochemically pure form.

Conclusion: Prunolactone A (**3b**) was thus prepared in a high overall yield of 11% from (–)-shikimic acid. Also, the 8-step synthesis of unnatural (3´*R*)-epimer of prunolactone A (**3a**), using (8*R*)-scytolide (**2a**) as a dienophile, was performed. The overall yield of this synthesis represents up to 19% from (–)-shikimic acid.



Scheme 1

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P09

SYNTHESIS AND REACTIVITY OF SUBSTITUTED TETRAHYDROPYRIDINES AS MASKED CYCLIC [3]DENDRALENES

Petr Matouš [1], Marek Timorácký [1], Jiří Kuneš [1], Milan Pour [1]

[1] Charles University, Faculty of Pharmacy in Hradec Králové, Czech Republic

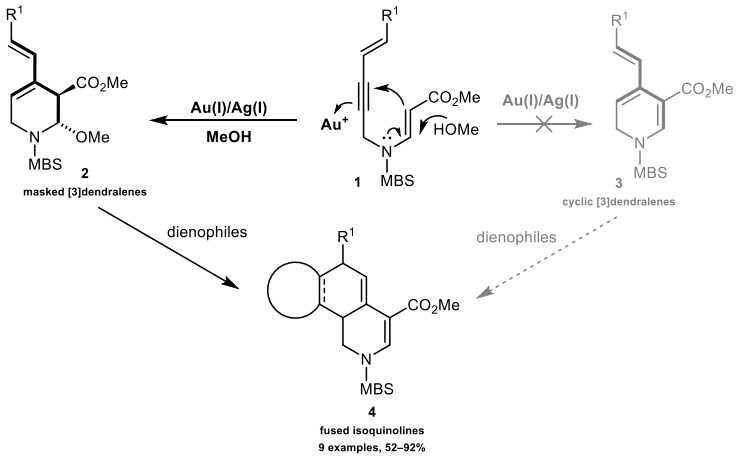
ABSTRACT

Objectives: Gold-catalyzed cyclization of the easily available 3-aza-1,5-enynes **1** provided substituted tetrahydropyridines **2** that can be considered masked cyclic [3]dendralenes **3**, whose direct synthesis was not successful. We aimed to prove the reactivity of tetrahydropyridines **2** in [4+2]cycloadditions.

Methods: 3-Aza-1,5-enynes were synthesized in 3-steps sequence and underwent gold-catalyzed cyclization in the presence of methanol as external nucleophile furnishing tetrahydropyrines **2**.

Results: Diels-Alder reaction of **2** with simultaneous elimination of methanol furnished a series of remarkable fused isoquinoline derivatives **4**.

Conclusion: This study proved the possibility of Diels-Alder cycloadditions of tetrahydropyridines prepared.



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P10

FROM CARLTONINE-TYPE ALKALOIDS TO SELECTIVE BUTYRYLCHOLINESTERASE INHIBITORS: DESIGN, SYNTHESIS, AND BIOLOGICAL EVALUATION

Filip Pidaný [1], Jana Křoustková [1], Xavier Brazzolotto [2], Martina Hrabinová [3], Lenka Pulkrábková [3], Jan Korábečný [3], Lucie Cahlíková [1]

[1] Department of Pharmacognosy and Pharmaceutical Botany, Faculty of Pharmacy in Hradec Králové, Charles University, Akademika Heyrovského 1203, 500 05 Hradec Králové, Czech Republic

[2] Institut de Recherche Biomédicale des Armées, Département de Toxicologie et Risques Chimiques, 1 Place Général Valérie André, 91220, Brétigny-sur-Orge, France

[3] Biomedical Research Center, University Hospital Hradec Králové, Sokolská 581, 500 05 Hradec Králové, Czech Republic

ABSTRACT

Objectives: The study aims to develop novel, highly selective butyrylcholinesterase (BChE) inhibitors with potential therapeutic applications in Alzheimer's disease (AD). BChE is substantially involved in AD pathophysiology, particularly in advanced stages, and is linked to non-cholinergic processes such as beta-amyloid aggregation and ghrelin metabolism.[1,2] Building on the plant alkaloid carltonine B as a lead structure, new compounds with enhanced CNS activity have been designed and synthesized. Key structural features for BChE selectivity and efficacy have been identified, and structure-activity relationships were elucidated.

Methods: Novel BChE inhibitors were designed, synthesized, and characterized using NMR, LC-MS,
and HRMS. Their inhibitory activity against human cholinesterases was assessed by the Ellman's method. The most potent compounds underwent enzyme kinetics and X-ray crystallography. Blood-brain barrier (BBB) permeability was evaluated using a parallel artificial membrane assay (PAMPA), and *in vitro* toxicity was profiled by the MTT assay.

Results: Dozens of new compounds were synthesized, with many exhibiting selective human BChE (*h*BChE) inhibition *in vitro*, ranging from micromolar to nanomolar concentrations. Compounds **II-87** (*h*BChE IC_{50} = 3.8 ± 0.2 nM) and **II-88** (*h*BChE IC_{50} = 5.7 ± 1.5 nM) demonstrated the highest potency. Compounds with sub-100 nM inhibition confirmed BBB permeability via the PAMPA assay and demonstrated favorable cytotoxicity in SH-SY5Y and HepG2 cell lines. Crystallographic study revealed key interactions between **II-87** and *h*BChE, elucidating its high inhibitory activity.

Conclusion: The development of novel selective *h*BChE inhibitors derived from the alkaloid carltonine B represents a step forward in developing potential therapies for mid- to late-stage AD.

The project New Technologies for Translational Research in Pharmaceutical Sciences /NETPHARM, project ID CZ.02.01.01/00/22_008/0004607, is co-funded by the European Union.

References:

1. Xing, S.; *et al*. *Med. Res. Rev.* 2021, *41*, 858-901.
2. Sun, T.; *et al*. *Eur. J. Med. Chem.* 2024, 275, 116569.

P11

Cooperative Chalcogen- and Hydrogen Bonding Catalyzed Asymmetric Thiol Addition

Jan Sokolov [1], Abhishek Bissoyi [1], Tomáš Hodík [1]

[1] Department of Organic and Bioorganic Chemistry, Faculty of Pharmacy in Hradec Králové, Charles University, Czech Republic

ABSTRACT

Objectives: Chalcogen bonding is an attractive interaction between an electrophilic region (σ-hole) of a chalcogen atom and a Lewis base. Potential applications of chalcogen bonding include anion transport and Lewis acid catalysis. Although it has been demonstrated that chalcogen bonding catalysis facilitates many chemical transformations, their application is limited to non-stereoselective catalysis so far. The objective is to prepare enantioselective chalcogen bonding catalysts and to investigate their applications.

Methods: The method is organocatalysis based on non-covalent interactions.

Results: We designed and synthesized a series of chiral catalysts, which could be applied for enantioselective chalcogen bonding catalysis. The catalysts are based on a chiral binaphthyl backbone, and they combine a cationic selenonium moiety as a chalcogen binding site with a hydrogen-bond-donating group (amide, squaramide or sulfonamide). The catalysts were assumed to mediate an addition of thiols to imines through the non-covalent interactions between the reagents and the chalcogen and hydrogen binding sites of the catalyst. The reaction proceeded in an enantioselective manner and provided enantiomerically enriched thioaminals in high yields. Furthermore, it was discovered that the enantioselectivity of the catalyst can be tuned by the presence of a suitable counteranion.

Conclusion: To conclude, we demonstrated that a chalcogen-bonding catalyst can be applied for asymmetric catalysis. We are planning to expand the methodology and use for synthesis of pharmaceutically relevant compounds such as thiazolidinones.

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P12

OSH6 MEDIATES LIPID TRANSPORT IN A MEMBRANE COMPOSITION-DEPENDENT MANNER

Alena Balleková[1], Andrea Eisenreichová[1], Evžen Bouřa[1], Jana Humpolíčková[1]

[1] Institute of Organic Chemistry and Biochemistry, Czech Academy of Sciences, Flemingovo nam. 2, 160 00 Prague, Czech Republic

ABSTRACT

Objectives: Non-vesicular lipid transport is essential for maintaining cellular lipid homeostasis and the distinct identities of individual membrane organelles. Oxysterol-binding protein-related proteins (ORPs) form a large family of proteins primarily functioning in this process. In general, these proteins act at membrane contact sites, shuttling lipids from donor to acceptor membranes through the cytosol via their lipid-binding hydrophobic pockets. In our study, we focus on a member of this family, Osh6, which is in yeast involved in the transport of phosphatidylserine (PS) from its site of synthesis in the endoplasmic reticulum (ER) to the plasma membrane against its concentration gradient. The main feature of the transport mechanism is the exchange between two cargo molecules, PS and phosphatidylinositol-4-phosphate (PI4P), with the latter being shuttled back to the ER. However, the exact mechanism remains unclear.

Methods: To investigate this, we developed an in vitro fluorescence cross-correlation spectroscopy assay to monitor lipid transfer using large unilamellar vesicles.

Results: Our results demonstrate that the occupation of Osh6 by a particular cargo lipid influences the recognition of a distinct target membrane, thereby determining the transport directionality. Additionally, we show that Osh6 tethers membranes in a manner dependent on lipid composition, confirming the crucial role of membrane physical properties, such as charge and fluidity, in this process.

Conclusion: These findings provide insights into lipid transfer mechanisms and the impact of Osh6 on membrane dynamics. Furthermore, Osh6's ability to modulate membrane composition suggests a broader role in regulating lipid-dependent cellular processes.

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P13

EMPLOYING CLICK CHEMISTRY FOR INTRACELLULAR CARGO DELIVERY

Oleh Durydivka, Marek Chovanec, Rastislav Dzijak, Michal Rahm, Jachym Hrusak, Paul Reyes, Milan Vrabel

Institute of Organic Chemistry and Biochemistry of the CAS, Flemingovo nám. 2, 16000, Prague (Czechia)

ABSTRACT

Objectives: Targeting small molecules to specific organelles holds significant potential for medical applications. Various strategies focus on delivering active drugs or fluorophores to intracellular compartments. Here, we exploit the bioorthogonal click chemistry reaction between *trans*-cyclooctene (TCO) and 1,2,4,5-tetrazine (Tz) to covalently link organelle-targeting probes with molecular cargos.

Methods: U2OS cells were sequentially incubated with organelle-targeting probes and fluorophores containing complementary click partners. Colocalization of the click products with organelle-specific markers was evaluated using confocal microscopy and image analysis.

Results: Selected organelle-targeting probes demonstrated precise localization to the plasma membrane, mitochondria, nucleus, endoplasmic reticulum, and lysosomes. However, certain combinations showed reduced organelle specificity or failed to produce detectable click products.

Conclusion: Our findings demonstrate that the TCO-Tz click reaction enables targeted delivery of molecular cargos to specific organelles. This reaction can alter cargo properties, facilitating changes in intracellular distribution. Bioorthogonal reactions may be a new means for more precise medicine. This approach may enhance drug delivery efficiency, minimize off-target effects, and enable controlled therapeutic interventions. Future studies could further refine the selectivity and efficiency of these reactions, broadening their potential applications in precision medicine and intracellular imaging.

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P14

SYNTHESIS AND INCORPORATION OF MODIFIED SIALIC ACIDS FOR CELL LABELLING

Anna Kovalová[a], Simona Bellová[a], Rastislav Dzijak[a], Milan Vrábel[a]

[a] Institute of Organic Chemistry and Biochemistry of the CAS, Prague, kovalova@uochb.cas.cz

ABSTRACT

Objectives: Sialic acid is uniquely suited for cell labeling, as it is typically the terminal unit of cell surface polysaccharides. When modified with a reactive dienophile moiety, it undergoes a rapid bioorthogonal inverse-electron-demand Diels–Alder (IEDDA) reaction with tetrazines. In this work, three derivatives of sialic acid were tested/compared as candidates for ChemCell technology.

Methods: We utilize chemical synthesis in tandem with metabolic glycoengineering (MGE) to incorporate modified sialic acids into cell structures. The engineered cells are then labeled with tetrazine-containing molecules.

Results: 2-*trans*-cyclooctene moiety emerged as the best dienophile reporter, ready for IEDDA reaction with tetrazines in concentrations as low as 2.5uM.

Conclusion: ChemCell labelling methodology is effective for conjugating both small and large molecules. Compared to established protocols, it demonstrates superior efficiency in ligating large active molecules, such as antibodies, at lower concentrations.

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P15

SEARCH FOR NOVEL CANCER THERAPEUTICS: INHIBITING KEY EPIGENETIC REGULATORS NNMT, PCIF1, AND DNMT1

Petr Škvára[1], Barbora Landová[1], Dominika Chalupská[1], Karel Chalupský[1], Jakub Benýšek[1], Radim Nencka[1], Evžen Bouřa[1]

[1] *Institute of organic chemistry and biochemistry of the Czech academy of Science, Flemingovo nam. 542/2, Praha 6, 166 10*

ABSTRACT

Objectives: Cancer, driven by genetic and epigenetic changes, remains a major cause of death worldwide. Targeting key regulatory enzymes offers new opportunities for therapy. Our goal is to prepare and characterize selected S-adenosyl-L-methionine (SAM)-dependent methyltransferases: nicotinamide N-methyltransferase (NNMT), phosphorylated CTD interaction factor 1 (PCIF1), and DNA methyltransferase 1 (DNMT1) and further evaluate their enzymatic activity and structural changes in presence of carefully selected potential inhibitors from our vast library of S-adenosylhomocysteine (SAH) analogues.

NNMT regulates cellular metabolism through nicotinamide methylation and is highly expressed in various cancers [1]. PCIF1 catalyzes m6Am modification of mRNA, influencing gene expression and promoting tumor progression [2]. DNMT1 maintains DNA methylation patterns, and its dysregulation leads to oncogenesis [3].

Methods: We use recombinant expression systems to produce selected methyltransferases, followed by purification with the ÄKTA Pure system using various chromatography techniques. Structural analysis, with and without bound inhibitors, is conducted using X-ray crystallography and cryo-EM. Enzymatic activity is assessed by measuring the reaction product SAH, using the ECHO mass spectrometry system. Substrates for enzymatic assays are either commercially synthesized or prepared in-house.

Results: So far we were able to prepare and purified all selected enzymes. We also conducted library screen of inhibitors prepared in-house with NNMT and have crystals of PCIF1 without inhibitor.

Conclusion: Our research aims to identify small-molecule inhibitors for these enzymes based on the methylation mechanism, we focus on analogs of SAH. We tend to characterize their binding mechanisms and evaluate their efficacy, providing a foundation for novel cancer therapies.

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P16

FOXO1-binding small molecules: computational challenges and opportunities

Wim Dehaen 1, Katarzyna Kwiecińska1 Pavla Perlíková1, Daniel Svozil2, Andrea Brancale 1

1 Department of Organic Chemistry, Faculty of Chemical Technology, University of Chemistry and Technology Prague, Technická 5, 16 628 Prague 6, Czech Republic;

2 Department of Informatics and Chemistry, Faculty of Chemical Technology, University of Chemistry and Technology Prague, Technická 5, 16 628 Prague 6, Czech Republic;

ABSTRACT

Objectives: Forkhead box protein Isoform 1 (FOXO1) is a transcription factor involved in a large amount of physiological processes, including glucose metabolism, apoptosis and stress resistance. Modulating its regulatory activity could thus affect various disease processes. However, this transcription factor is a classic example of an "undruggable protein": there is no tractable small molecule binding site, its DNA binding domain (DBD) surface is shallow and not pocket-like, and a large portion of the protein structure is disordered. Known FOXO1 inhibitors have serious shortcomings. For example, the commonly used FOXO1-inhibiting small molecule AS1842856 suffers from poor solubility, low selectivity over other FOXO isoforms, and a promiscuous fluoroquinolone scaffold. Our objective is to understand small molecule engagement with FOXO1 better in order to pick appropriate methods to design better FOXO1 modulators.

Methods: Site Detection algorithms such as SiteFinder and P2Rank. Co-folding with Protenix and Chai-1.

Results: Site Detection algorithms confirm there are no reasonable small molecule binding sites in the structured part of FOXO1, the DBD. Co-folding with Protenix leads to a structure with excellent agreement with experimental data, but also outputs nonsensical data for the disordered region and places the ligand in an unlikely region. Co-folding with Chai-1 suggests AS1842856 might engage the DBD via interactions with Lys101, Arg10 and Ser65, offering an unlikely but testable binding hypothesis.

Conclusion: We confirm standard structure-based virtual screening methods are not fruitful here. Co-folding methods offer a promising alternative, but generate unrealistic output that requires human intervention.

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P17

Selective Formation of Coamorphous Systems with Enzalutamide: Benzene Rings as Key Structural Features

Argyro Chatziadi [1], Kateřina Neubergerová [1], Dan Trunov [1], Venkata Balaga [1], Luděk Ridvan [2], Miroslav Šoóš [1]

[1]Department of Chemical Engineering, University of Chemistry and Technology in Prague, Technická 3, 16628, Prague 6, Czech Republic

[2]Zentiva k.s., U Kabelovny 130, 10237, Prague 10, Czech Republic

ABSTRACT

Objectives: Enzalutamide (ENZ), a non-steroidal antiandrogen used in the treatment of metastatic castration-resistant prostate cancer, exhibits poor aqueous solubility and bioavailability, limiting its therapeutic efficacy. The aim of this study is to investigate the formation mechanism and properties of coamorphous systems of ENZ with small organic acids and amino acids.

Methods: In this study, ball milling was used to investigate the formation of coamorphous systems of ENZ with 6 amino acids, including L-phenylalanine (PHE), L- tryptophan (TRY), L-proline (PRO), L-Leucine (LEU), L- Methionine (METH) and L-Valine (VAL), and 8 carboxylic acids including 2-aminobenzoic acid (2AA), 2,5- dihydroxybenzoic acid (25H), salicylic acid (SAL), benzoic acid (BEN), pimelic acid (PI), adipic acid (AD) , glutaric acid (GLU) and succinic acid (SUC). The new coamorphous systems were characterized by Powder X-ray Diffraction (XRPD), Modulated Differential Scanning Calorimetry (mDSC) and Attenuated total reflection Fourier transform infrared spectroscopy (ATR-FTIR).

Results: The formation of six coamorphous systems was confirmed by XRPD and mDSC measurements. Notably, coamorphous systems were successfully formed only with coformers containing a benzene ring, including BEN, SAL, 2AA, 25H, PHE and TRY, suggesting a critical role of aromaticity in stabilizing the amorphous phase. Thermal analysis and dissolution studies revealed that the coamorphous systems exhibited enhanced glass transition temperatures (Tg) and significantly improved dissolution rates compared to crystalline ENZ.

Conclusions: These findings underscore the importance of molecular structure of both API and coformer in coamorphous system formation but also provide a targeted approach for selecting suitable coformers to optimize the physicochemical properties of Enzalutamide.

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P18

SYNTHESIS OF SMALL MOLECULES BINDING TO RNA WITH ANTIVIRAL POTENTIAL

Obertík R.,[1] Harvalík J.,[1] Brossard S.,[1] Mathez G.,[2] Cuřínová P.,[1] Cagno V.,[2] Brancale A.[1]

[1] *Department of Organic Chemistry, University of Chemistry and Technology, Prague, 166 28, Czech Republic*

[2] *Institut de Microbiologie , Centre Hospitalier Universitaire Vaudois, Lausanne, 1011, Switzerland*

ABSTRACT

Objectives: In this work, we are presenting the synthesis of a series of novel molecules based on Merafloxacin, designed to bind to RNA, which can work as Inhibitors of PRF or RNA degraders. Additionally, the compounds were also tested against SARS-CoV-2 and in a specific assay to measure the PRF.

Methods: The synthesis provided novel molecules with a fluoroquinolone skeleton, which were analyzed via NMR and UPLC/MS. Biological assays were done in collaboration with a partner laboratory in Switzerland.

Results: The small library of fluoroquinolone derivatives was synthesized and tested in antiviral activity.

Conclusion: Based on Merafloxacin, 15 novel molecules were synthesized. Biological assays have shown antiviral activity in 2 compounds.

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P19

SIMULTANEOUS DETERMINATION OF THERAPEUTIC MONOCLONAL ANTIBODIES AND THEIR NEUTRALIZING ANTIBODIES BY UHPLC-MS/MS

Veronika Pilařová [1], Kateřina Plachká [1], Irena Murínová [2,3], Luce Nováková [1]

[1] Department of Analytical Chemistry, Faculty of Pharmacy in Hradec Králové, Charles University, 50003 Hradec Králové, Czech Republic

[2] Department of Social and Clinical Pharmacy, Faculty of Pharmacy, Charles University, Czech Republic

[3] Department of Clinical Pharmacy, Military Faculty Hospital Prague, Prague, Czech Republic

ABSTRACT

Objectives: The use of therapeutic monoclonal antibodies (mAbs) has steadily increased in the development of modern treatment strategies for various diseases. Despite their benefits, their use can trigger an immune response, resulting in the production of anti-drug antibodies. Indeed, neutralizing antibodies inhibit the binding of mAbs to the target structure, potentially causing treatment failure.

Methods: The trypsin digestion of adalimumab, infliximab, and dupilumab was carried out to obtain proteotypic peptides. The samples were analyzed using ultra-high performance liquid chromatography with tandem mass spectrometry (UHPLC-MS/MS). The 3 min separation was carried out on CSH C18 stationary phase (2.1 x 100 mm, 1.7 µm) and gradient elution of aqueous 0.02% propionic acid in ACN with 0.02% propionic acid.

Results: The first step of the study aimed at the UHPLC-MS/MS optimization, including (i) the selection of stationary phase, (ii) optimization of the mobile phase composition, i.e., type and concentration of acid added to the organic and aqueous part, (iii) optimization of the gradient elution, (iv) parameters of the electrospray ionization source, and (v) selective reaction monitoring (SRM) transitions for each mAb. The second part has been focused on the mAbs enzymatic digestion procedure with an emphasis on the increased recovery of mAbs. Effect of the buffer, guanidine, and trypsin concentration have been studied.

Conclusion: The obtained results will be used to develop a simple universal approach for analysis and quantification of various mAbs and their neutralizing antibodies, which will be used in clinical practice to appropriately adjust the therapeutic window in personalized medicine.

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P20

GLUCOCORTICOID-LOADED PLGA NANOSPHERES FOR MACROPHAGE TARGETING: A NOVEL APPROACH FOR INFLAMMATION MANAGEMENT

Barbora Boltnarová [1], Ondřej Holas[1], Petr Pávek [2]

[1] Department of Pharmaceutical Technology, Faculty of Pharmacy in Hradec Králové, Charles University, Czech Republic

[2]Department of Pharmacology and Toxicology, Faculty of Pharmacy in Hradec Králové, Charles University, Czech Republic

ABSTRACT

Objectives: Nanotechnology enables precise drug delivery, improving therapeutic efficacy while minimizing side effects. Liver inflammation remains a global health challenge, requiring innovative treatments. Glucocorticoids are potent anti-inflammatory agents, but their non-specific distribution leads to severe side effects. Macrophages play a key role in inflammation, making them ideal targets for glucocorticoid therapy. This study aimed to develop biodegradable poly(lactic-co-glycolic) acid (PLGA) nanospheres (NSs) for targeted glucocorticoid delivery to liver macrophages, enhancing treatment safety and efficacy.

Methods: Dexamethasone acetate (DA)-loaded NSs were prepared using the nanoprecipitation method. Two types of DA NSs, ranging in size from 100 to 200 nm, were synthesized, achieving a maximum DA loading efficiency of 20% and a sustained drug release over three days. The anti-inflammatory effects of DA-loaded NSs were evaluated using macrophage cell lines (BMM, THP-1, J774.2) by analyzing the gene expression of pro-inflammatory cytokines (*Tnf-α*, *Il-1β*) through RT-qPCR. *In vivo* studies in murine models assessed liver-specific DA-loaded NSs accumulation using flow cytometry, IVIS imaging, and fluorescence microscopy of tissue slides.

Results: DA-loaded NSs demonstrated efficient macrophage uptake, significant suppression of pro-inflammatory cytokines (*Tnf-α, Il-1β*), and no cytotoxicity in all macrophage cell lines used. *In vivo*, NSs selectively accumulated in liver macrophages following intravenous administration.

Conclusion: PLGA-based NSs provide a promising targeted glucocorticoid delivery system, enhancing therapeutic efficacy while reducing systemic side effects, offering safer and more effective glucocorticoid therapy.

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P21

PHENOLIC ACID BASED COAMORPHOUS FORMS OF NON-STEROIDAL ANTIANDROGEN DRUG ENZALUTAMIDE

Venkata Krishna Rao Balaga [1], Agyro Chatziadi [1], Ludek Ridvan [2], Miroslav Šoóš [3]

[1] Department of Chemical Engineering, University of Chemistry and Technology, Technická 3, 166 28 Prague 6 – Dejvice, Czech Republic.

[2] Zentiva, k.s., U Kabelovny 130, 10237 Prague 10, Czech Republic.

ABSTRACT

Objectives: Enzalutamide (ENZ) categorized as a BCS class II drug is a nonsteroidal antiandrogen drug. It exhibits low bioavailability due to its poor aqueous solubility and dissolution profiles. This study aimed to use phenolic acids as potential coamorphous co-formers to improve the physicochemical properties of the drug enzalutamide.

Methods: In this study, five phenolic acids, including p-coumaric acid (CMA), ferulic acid (FRA), cinnamic acid (CNA), vanillic acid (VNA), and p-hydroxybenzoic acid (HBA) were used as potential coamorphous coformers to prepare binary ENZ-Co-former coamorphous formulations. These new coamorphous systems were characterized by powder X-ray diffraction (PXRD), the modulated temperature differential scanning calorimetry (mDSC), Attenuated total reflectance Fourier transform infrared spectroscopy (ATR-FTIR), and Raman spectroscopy.

Results: The formation of coamorphous forms was confirmed by the absence of diffraction peaks in the XRPD spectra, as well as the appearance of a single Tg in the mDSC. ATR-FTIR analysis and Raman spectroscopy suggested the lack of intramolecular interactions in the prepared coamorphous forms. Compared to the crystalline ENZ, the coamorphous forms exhibited superior solubility rates over the entire range of physiological pH conditions. Moreover, the drug in coamorphous forms exhibited a significant increase in the intrinsic dissolution rate and could maintain supersaturation for at least 6 hours, in non-sink conditions. In addition, the coamorphous forms exhibited improved physical stability under higher humidity conditions.

Conclusion: The results of these studies may offer a promising platform for further use of phenolic acid as a potential coamorphous co-former for improving the physicochemical properties of active pharmaceutical ingredients (APIs).

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P22

PREPARATION AND APPLICATIONS OF PHARMACEUTICAL NANOCRYSTALS

Chvíla S.[1], Hampl V.[1], Klimša V.[1], Mutylo E.[1], Štěpánek F[1].

[1]University of Chemistry and Technology Prague, Department of Chemical Engineering, Technicka 3, 160 00 Praha 6, Czech Republic

ABSTRACT

Objectives: Our main objective is to determine the viability of solid nanocrystal-containing forms of varied drug loading, using both different nanocrystal stabilizers and different fillers of the solid matrix. We consider this formulation step to be a significant step towards creating highly efficacious drug carriers.

Methods: Lab-scale screening of top-down drug nanomilling was done as previously communicated, including subsequent morphological and XRPD analysis. Three model drugs were chosen from the previously used set as model drugs for further tests of solidification approaches: spray drying and lyophilisation.

Results: Aqueous nanosuspensions stabilized by HPMC E5 and SLS were prepared in laboratory scale, achieving mean volume sizes in hundreds of nm. All suspensions remained stable after 12 months of storage. Lyophilized and spray-dried nanosuspensions were prepared, yielding homogeneous, non-hydrophobic powders. Standardized dissolution tests indicated improved dissolution properties of spray-dried powders.

Conclusion: Successful preparation of well-described solid form nanocrystals of multiple drugs was achieved and described, while preserving their original crystal form. The authors see future prospects of this work in upcoming attempts to establish solid-form nanocrystals as a platform technology in drug development and preformulation.

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P23

HYALURONIC ACID AS VEHICLE FOR DELIVERY OF NANOCRYSTALS CAPABLE OF ENHANCING IMIQUIMOD SKIN BIOAVAILIBITY

Vendula Janoušková [1], Kateřina Čermáková [1], Eliška Kurfiřtová [1], Jarmila Zbytovská [1]

[1] Dept. Org. Technol., UCT Prague, Technická 5, 166 28 Praha-Dejvice, Czechia

ABSTRACT

Objectives: Dermal drug delivery remains challenging due to low drug solubility and poor skin bioavailability. One example of such troublesome drug is imiquimod, which is commonly used to treat actinic keratosis and basal cell carcinoma. In recent years, we have developed several promising nanoparticles that have proven effective in dermal delivery. However, their use in clinical practise is still questionable due to their low viscosity. Therefore, finding a suitable nanocarrier vehicle is essential for the next step in our research. One of the ideal candidates is hyaluronic acid (HA) due to its unique biological functions.

Methods: Nanocrystals (NC) were prepared by wet milling and characterized by dynamic light scattering and transmission electron microscopy. The viscosity of the NC-HA gels composed of different molecular weight of HA was determined. Furthermore, the efficacy of NC-HA gels in imiquimod delivery was proved in *ex vivo* permeation study on porcine skin.

Results: Of all the tested HA types, the NC-HA gel with the molecular weight 1 MDa achieved the best skin delivery of imiquimod. In fact, in term of solubility and skin bioavailability, the obtained results were even better than those for a commercial imiquimod-based cream. Additionally, this NC-HA gel showed good stability and suitable rheological properties for skin application.

Conclusion: NC-HA gel based on 1 MDa HA shows considerable promise for dermal drug delivery of imiquimod making it a potential candidate for clinical use.

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P24

ORALLY DISPERSIBLE FILMS

Petr Jelínek[1], Dominik Švára[1], Miroslav Šoóš[1]

[1] Department of Chemical Engineering, University of Chemistry and Technology Prague, Technická 3, 166 28 Prague 6, Czechia

ABSTRACT

Objectives: This study aims to develop a novel method for preparing porous orally dispersible films (ODFs) to enhance ease of use and improve patient compliance with therapy.

Methods: We modified the solvent casting technique to integrate a porogen insoluble in organic solvent, which was removed through film heating and thermal decomposition. Parametric studies investigated the impact of various formulation components, including the porogen, drug, disintegrant, and the ratio of film former to thickener on film properties.

Results: The study found a significant correlation between porosity and disintegration time. Disintegration time decreased from 53.9 ± 2.4 seconds for samples with a porogen mass ratio of 0.28 to 4.3 ± 0.1 seconds for samples with a porogen mass ratio of 0.73. The presence and removal of the porogen did not interfere with the incorporated model API or produce any toxic byproducts.

Conclusion: The novel method for preparing porous ODFs is viable and offers an alternative to current pharmaceutical forms, enhancing the processability and disintegration properties without compromising the safety and efficacy of the incorporated API.

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P25

Investigation of physicochemical properties of cannabidiol cocrystals

Adéla Koryťáková[1], Argyro Chatziadi[1], Jan Rohlíček[2], Eliška Zmeškalová[2], Josef Beránek[3], Miroslav Šoóš[1]

[1]Department of Chemical Engineering, University of Chemistry and Technology in Prague, Technická 3, 16628, Prague 6, Czech Republic

[2]Institute of Physics of the Czech Academy of Sciences, Na Slovance 2, 182 00, Prague 8, Czech Republic

[3]Zentiva k.s., U Kabelovny 130, 10237, Prague 10, Czech Republic

ABSTRACT

Objectives: Cannabidiol (CBD), a natural compound found in *Cannabis sativa*, exhibits significant therapeutic potential in the treatment of various pathological conditions, including pain, nausea, cancer, and neurodegenerative disorders. Despite its promising applications, CBD faces significant challenges for oral administration, primarily due to its low solubility, low melting point (67 °C), and poor stability. This study aimed to enhance the physicochemical properties of CBD through cocrystal screening.

Methods: The cocrystal screening was carried out using two solvent-based methods namely slurry and milling, leading to the formation of five CBD cocrystals. The solid forms were characterized through X-ray powder diffraction, differential scanning calorimetry, and nuclear magnetic resonance. Intrinsic dissolution rates were measured for all multicomponent forms. Furthermore, the accelerated stability study was conducted to predict degradation behaviour of the cocrystals.

Results: The prepared cocrystals exhibited increased melting points compared to the pure CBD. The crystal structures of three cocrystals were solved and used to understand their stability and degradation behaviour under accelerated conditions. Stability testing demonstrated that CBD-4,4'-bipyridine and CBD-L-proline cocrystals exhibited greater stability and resistance to degradation under accelerated stress conditions compared to pure CBD.

Conclusion: The cocrystallization enhanced the thermal stability of CBD. Furthermore, our findings reveal that the melting point is not the only determining factor for cocrystal stability and it is important to consider also other factors, including interaction energies of the molecules, surface morphology and hygroscopicity of the crystals. Among the tested cocrystals, CBD-L-proline showed promising stability, suggesting its potential for pharmaceutical development.

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P26

Imiquimod nanosystems for advanced dermal delivery

Eliška Kurfiřtová[1], Stanislav Chvíla[1], Martin Balouch[1], Jarmila Zbytovská[1]

[1]University of Chemistry and Technology Prague, Technická 5, 16628 Prague, Czech Republic

ABSTRACT

Objectives: Imiquimod (IMQ) is commonly used in the treatment of precancerous skin conditions but has low bioavailability because of the poor solubility in most pharmaceutical excipients. Our study aims to enhance the bioavailability and therapeutic efficiency of IMQ with a novel nanosystem that balances skin adhesion, deeper skin penetration, and reduced systemic effects.

Methods: Nanosystems (liposomes, lipid nanocapsules, nanoemulsions, and nanocrystals) were prepared using standard methods such as thin film hydration, high pressure, shear homogenization, or wet milling. The ability of these nanosystems to deliver IMQ into skin tissue was demonstrated through *ex vivo* studies on porcine skin.

Results: The encapsulation of IMQ in various nanosystems yielded different levels of efficacy, but all were successful in the *ex vivo* study. The nanoemulsion delivered the highest amount of IMQ followed closely by nanocrystals against the Aldara® cream used as a control in this study. On the contrary, liposomes and lipid nanocapsules released lower concentrations of IMQ, primarily due to their low IMQ content.

Conclusion: Two nanosystems, nanoemulsion and nanocrystal, were selected as lead formulations in extensive studies focusing on the physicochemical characterization of nanosystems (e.g. size, morphology, and encapsulation efficacy) and their ability to deliver IMQ into skin tissue in *ex vivo* studies.

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P27

NANOPARTICULATE SYSTEMS FOR DERMAL DELIVERY OF ANTIMYCOTICS

Damla Orhan[1,2], Stanislav Chvíla[1], Josef Beránek[2], Jarmila Zbytovská[1]

[1]University of Chemistry and Technology in Prague, Department of Organic Technology, Technická 5, 16628, Prague 6, Czech Republic, orhand@vscht.cz, chvilas@vscht, zbytovsj@vscht.cz

[2] Zentiva k.s., U Kabelovny 130, 10237, Prague 10, Czech Republic, Josef.Beranek@zentiva.com

ABSTRACT

Objectives: Fungal skin infections are a widespread health concern, often requiring prolonged treatment with conventional antifungal drugs that may have limited efficacy and low bioavailability, leading to suboptimal therapeutic outcomes. This study aims to develop and characterize itraconazole (ITZ)-loaded nanoparticulate systems (polymeric, lipid-based, and nanocrystals) to enhance skin delivery, improve therapeutic efficacy, and potentially reduce adverse effects.

Method: Five different ITZ-loaded nanoparticulate systems were developed using nanoprecipitation, high-shear homogenization, and wet-milling methods. The systems were characterized for particle size, polydispersity index (PDI), zeta potential, surface morphology, drug loading, and entrapment efficiency using DLS, SEM, TEM, and HPLC. *In vitro* drug release and *ex vivo* skin permeation studies were conducted to assess drug release, skin penetration, and potential therapeutic efficacy.

Results: All developed NPs (PLGA, nanoemulsions, and nanocrystals) exhibited desirable particle size (<300 nm), narrow size distribution (PDI < 0.25), high drug encapsulation efficiency (90–100%), and stability after production. *Ex vivo* permeation studies revealed that ITZ nanocrystals achieved the highest dermal entrapment compared to other formulations, suggesting enhanced skin delivery potential.

Conclusion: We developed ITZ-loaded nanoparticulate systems using scalable and eco-friendly methods. ITZ nanocrystals emerged as the most promising nanoparticles for dermal drug delivery due to their superior skin entrapment. These findings lay the groundwork for future studies to investigate the skin penetration mechanisms of nanoparticulate systems, paving the way for more effective topical antifungal therapies.

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P28

CERAMIDE EOP ENRICHED CEROSOMES FOR ADVANCED THERAPY OF SKIN DISEASES

Nikola Strnádková[1], Jarmila Zbytovská[1]

[1]Dept. Org. Technol., UCT Prague, Technická 5, 166 28 Praha, Czechia

ABSTRACT

Objectives: Skin diseases such as psoriasis or atopic dermatitis are related to a damaged skin barrier and reduced ceramide levels in the *stratum corneum* (SC). Direct ceramide administration offers an alternative to corticosteroids but faces challenges due to ceramides´ poor solubility and low bioavailability into the skin. Our research team has introduced cerosomes (CRs), vesicular lipid carriers mimicking SC lipid composition, to effectively deliver ceramides directly into the skin. Previously, CRs contained only common ceramides (NP and AP). The current goal is to enhance CRs with ceramide type EOP, which is significantly reduced in diseased SC. Moreover, the EOP is extremely rigid, crystalline and poorly soluble, making its incorporation into CRs challenging.

Methods: EOP-enriched CRs (EOP-CRs) were prepared by thin lipid film hydration and characterized by size. For the determination of morphology and lipid crystallinity optical and transmission electron microscopy were used. Efficacy in SC barrier function recovery was verified by an *ex vivo* skin restoration test on chemically damaged porcine skin, modeling diseased human skin.

Results: EOP-CRs were successfully developed with a total lipid content of 1 %. This formulation did not include any crystal fraction. The *ex vivo* skin restoration study proved the importance of EOP in the formulation compared to commonly used ceramides NP and AP, even in the very low concentration (0.07 % in total).

Conclusion: In summary, EOP-CRs were found to be successful in skin restoration compared to a simple suspension of EOP. This upgraded formulation has high potential to improve treatment of skin diseases.

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P29

Characterization of Amorphous Ibrutinib Thermal Stability

Dan Trunov [1], Jan Ižovský [1], Josef Beranek [2], Ondřej Dammer [2], Miroslav Šoóš [1]

[1] Department of Chemical Engineering, University of Chemistry and Technology, Technická 3, 166 28 Prague 6 – Dejvice, Czech Republic

[2] Zentiva, k.s., U Kabelovny 130, 102 00, Prague 10, Czech Republic

ABSTRACT

Objectives: The amorphization of Ibrutinib can improve its solubility and bioavailability, but its stability remains a key challenge. This study evaluates various amorphization techniques and investigates the impact of temperature on physicochemical properties, degradation pathways, and potential polymerization of degradation products.

Methods: Amorphous Ibrutinib was prepared using melt-quench, hot melt extrusion, solvent evaporation, ball milling, and lyophilization. The resulting materials were analyzed for changes in stability and degradation behavior. Thermal analysis was performed to assess the influence of temperature on solubility and permeability. Additionally, molecular weight changes due to degradation product polymerization were evaluated using Zimm plot analysis, a novel approach for this compound class.

Results: Temperature was identified as a **critical factor** influencing solubility, permeability, and degradation. A specific degradation product was observed to **polymerize**, leading to an increase in molecular weight. The polymerization rate and impurity structure were temperature-dependent, affecting the stability of amorphous Ibrutinib. Zimm plot analysis successfully determined the molecular weight of the degradation product, marking its first application in this context.

Conclusion: The choice of amorphization technique and temperature control plays a **crucial role** in the stability of amorphous Ibrutinib. Temperature-dependent polymerization of degradation products can significantly impact drug performance. Understanding these factors can aid in optimizing formulation strategies to enhance stability and efficacy.

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P30

NIR used as PAT for pharmaceutical industry

Adam Waněk [1], František Štěpánek [1]

[1] UCT Prague

ABSTRACT

Near-Infrared (NIR) Spectroscopy has emerged as a powerful Process Analytical Technology (PAT) tool for real-time monitoring and control of pharmaceutical and biopharmaceutical manufacturing processes. As a non-destructive and rapid NIR spectroscopy provides valuable insights into critical quality attributes (CQAs) and process parameters, ensuring compliance with Quality by Design (QbD) principles. The ability of NIR to analyze chemical composition, physical properties, and polymorphic forms in solid, liquid, and semi-solid formulations makes it highly versatile. By integrating NIR with multivariate data analysis (MVDA), scientists can gain deeper process understanding, optimize production quality, and minimize batch-to-batch variability.

Objectives: *NIR PAT can be used as a qualitative as well as quantitative analysis tool. Key applications described in this poster include both approaches*

Methods: Near-infrared spectroscopy paired with multivariate data analysis is used.

Results: Exploratory analysis together with real time monitoring is presented

Conclusion: Near-Infrared (NIR) spectroscopy is already transforming pharmaceutical Quality Control (QC) by shifting from traditional, time-consuming testing methods to real-time, non-destructive process monitoring. NIR is in comparison to traditional QC more efficient and provides more reliable quality assurance, leading to higher productivity and compliance with modern regulatory standards.

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P31

Drug Nanocrystals as a Tool for Effective Inhalational Drug Delivery

Denisa Lizoňová[1], Kateřina Slaninová[1], Michael Křivan[1], Hana Moravčíkova[1], Lenka Vyhlídalová[1]

[1] Chemical Robotics Laboratory, Department of Chemical Engineering, University of Chemistry and Technology Prague

ABSTRACT

Objectives: Oral drug delivery is inefficient for many lipophilic drugs due to poor solubility and first-pass metabolism, leading to low bioavailability and high dosing requirements. This study explores the potential of drug nanocrystals (DNCs) for inhalational delivery to improve systemic bioavailability, reduce dosing, and enhance therapeutic effects.

Methods: DNCs were prepared by wet milling using phospholipids (dipalmitoylphosphatidylcholine, dipalmitoylphosphatidylglycerol) as stabilizers, producing stable aqueous dispersions with high drug loading. Curcumin was used as a model drug due to its poor aqueous solubility. Size and stability were characterized by dynamic light scattering (DLS). Aerosolization efficiency was tested using a medical nebulizer and a cascade impactor.

A549 alveolar cells were cultured on Transwell inserts at the air-liquid interface (ALI) to develop a lung model. Monolayer formation was confirmed by confocal microscopy, with tight junction integrity evaluated using transepithelial electrical resistance (TEER) and fluorescence labeling. Absorption and translocation of nanocrystals will be assessed using a solvatochromic method.

Results: DNCs exhibited a mean size of ~100 nm with high colloidal stability. Aerosolized DNCs produced particles within the 2–5 µm range, ideal for pulmonary deposition. A549 cells formed intact monolayers and expressed tight junction proteins, confirmed by TEER measurements.

Conclusion: DNCs demonstrate significant potential for improving the bioavailability of poorly soluble drugs through inhalational delivery. This approach enables rapid absorption into systemic circulation while reducing dosing and potential side effects. Future work will focus on optimizing the lung model and evaluating both drug dissolution and solid particle translocation under physiologically relevant conditions.

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P32

Hepatorenal Syndrome: Safety and Efficacy of Pharmacotherapy—Findings from a Systematic Literature Review

E. Dvorackova[1,2], R. Mullerova[1], A. Zdobinska[1], H. Gottfriedova[3], S. Byrne[4], D. Fialova[1,5]

[1]Department of Social and Clinical Pharmacy, Faculty of Pharmacy in Hradec Kralove, Charles University, Hradec Kralove, Czech Republic

[2]Department of Pharmacology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic

[3]Institute for Clinical and Experimental Medicine, Prague, Czech Republic

[4]School of Pharmacy, University College Cork, Cork, Ireland

[5]Department of Internal Medicine and Geriatrics, 1st Faculty of Medicine, Charles University, Prague, Czech Republic

ABSTRACT

Objectives:
Hepatorenal syndrome (HRS) is a severe complication of cirrhosis, characterized by renal vasoconstriction and systemic vasodilation. Current therapeutic options remain suboptimal, particularly in older patients, an understudied population. This systematic literature review evaluates the safety and efficacy of HRS drug treatment strategieswhile identifying gaps in current guidelines.

Methods:
A systematic literature review was conducted using PubMed and Web of Science (2010–2024). The search included *'hepatorenal syndrome' OR 'hepato-renal syndrome'* with therapy-related terms. Eligible studies comprised systematic reviews, meta-analyses, and guidelines, while animal studies, pediatric clinical case studies, and non-European/American publications were excluded. A postdoctoral researcher independently reviewed identified guidelines (e.g. EASL (European Association for the Study of the Liver), NKF (National Kidney Foundation), and AASLD (American Association for the Study of Liver Diseases)) for consensus and discrepancies.

Results:
Of 1,286 identified records, 85 were included (72 systematic reviews/meta-analyses, 13 guidelines). Terlipressin with albumin is currently the first-line therapy for HRS-AKI (acute kidney injury), with norepinephrine as an alternative. In HRS-CKD (chronic kidney disease), RAAS inhibitors show promise. Preventive strategies include cautious diuretic use, nephrotoxic drugs avoidance, and hemodynamic stabilization. There is a lack of data on older patients, and current guidelines do not address medication safety and individualization of drug schemes of co-administered medications.

Conclusion:
The current HRS guidelines lack specificity in patient stratification and individualized therapeutic approaches. Critically, there is a substantial paucity of data on older and multimorbid patients, which hampers evidence-based clinical decision-making in this high-risk population.

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P33

Guidelines on the cardio-renal syndrom and aspects of rational pharmacotherapy

Jana Gregorová* (1,2), Veronika Krejčová (1), Simona Hlavatá (1), Milada Halačová (1,3) Sylvie Dusilová-Sulková (4), Daniela Fialova (1,5)

1 Department of Social and Clinical Pharmacy, Faculty of Pharmacy in Hradec Králové, Charles University

2 Department of Clinical Pharmacy, Na Bulovce Hospital, Prague

3 Department of Clinical Pharmacy, Nemocnice Na Homolce, Prague

4 Department of Nephrology, Faculty Hospital, Hradec Králové

5 Department of Internal Medicine and Geriatrics, 1st Faculty of Medicine. Charles University,

Prague, Czech Republic

ABSTRACT

Objectives: Cardiorenal syndrome (CRS) gained attention in the past decades due to significant impact on patients´ morbidity, mortality and quality of life, as well as due to the fact that drug regimens in patients with CRS should be highly individualized. The aim of this systematic literature review was to identify existing information in guidelines on CRS and individualized pharmacotherapy and drug classes discussed in these guidelines.

Methods: PubMed and WoS were searched for relevant article published (by Dec 2024). The search included key words „cardiorenal syndrom“ (+synonyma) AND „aged“ (+synonyma) AND „drug therapy“ (+synonyma). Only reviews and guidelines were selected based on inclusion criteria, other articles (e.g. animal studies, case reports, studies of other designs etc.) were excluded. Selected guidelines were independently reviewed by senior researchers.

Results: In PubMed we identified 1678 records, in WoS 2899 (in total 4577). After removing duplicates (1541), 3036 records were screened by 2 independent researchers and 1944 excluded as unrelated articles. After reading abstracts, 617 reviews and 7 professional guidelines were identified. The guidelines have been published between 2019-2024 by the American Heart Association, European Society of Hypertension, American Kidney Disease Improving Global Outcomes expert group, European society of cardiology and French Society of Cardiology. Drug classes discussed were mostly: ACEi, ARB, ARNI, SGLT2i, GLP-1 agonists, MRA, statins, ezetimibe, fibrates, BB, icosapent-ethylens, diuretics, MRA, digoxin, ivabradine,, vericiguat, isosorbide dinitrate, hydralazine, tolvaptan, DPP-4i, nephrotoxic drugs and iron.

Conclusion: Except cardiovascular medications, antidiabetics, nephrotoxic drugs and iron, other medications and principles of how to individualized their drug schemes in complex older adults are not stated in current guidelines. Guidelines always mostly focus on indicated drug treatment, but not on the safety of co-administered drugs for other co-morbidities.

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P34

Hepatorenal syndrom and current evidence on how to individualize drug schemes in older patients: findings from the systematic literature review

Milada Halačová (1,2)*, Adéla Zdobinská (1) , Regina Müllerová (1), Halima Gottfriedová (3), Eliška Dvořáčková (4), Sylvie Dusilová-Sulková (5), Daniela Fialova (1,6)

1 Department of Social and Clinical Pharmacy, Faculty of Pharmacy in Hradec Králové, Charles University

2 Department of Clinical Pharmacy, Nemocnice Na Homolce, Prague

3 Department of Hepatology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic

4 Department of Pharmacology, 1st Faculty of Medicine, Charles University

5 Department of Nephrology, Faculty Hospital Hradec Králové, Hradec Králové

6 Department of Internal Medicine and Geriatrics, 1st Faculty of Medicine. Charles University,

Prague, Czech Republic

ABSTRACT

Objectives: Methods on how to individualize drug schemes in complex older patients according to cardio-hepato-renal functioning are not yet sufficiently described in available guidelines. The aim of this systematic literature search was to identify current recommendations on how to individualize drug schemes in older adults with hepatorenal syndrome.

Methods: PubMed and Web of Science databases were used for this systematic literature search by applying synonyms of „hepatorenal syndrom“ AND „pharmacotherapy“ (+synonyms) AND „older adults“ (+ synonyms). All records were screen for relevancy by two independent researchers and discrepancies were resolved by the third senior reviewer.

Results: Primary search yielded in total 5816 records. After removing duplicates, 4679 records remained and in total 1373 studies were screen (by reading abstracts) for the latest period 2019-2024. 73 systematic or other literature reviews were identified (25 meta-analyses, 17 narrative reviews, 11 systematic literature reviews and 20 unspecified reviews). Drugs/drug classes mostly stated in these reviews were: terlipressin, albumin, noradrenaline, midodrine, vasoactive drugs, diuretics, antibiotics, beta-blockers and less frequently also NSAIDs, laxatives, antiviroticss, corticosteroids, imunosuppressants, cytostatics and hepatoprotective agents.

Conclusion: Until now, no systematic literature reviews or reviews were published on principles of how to individualize drug schemes in multimorbid older patients with hepatorenal syndrom. Clinical pharmacists due to their expertise may help to create such novel guidelines and to identify steps (using published literature evidence) of the individualization of frequently co-administed drugs in older adults in different stages of cardio-hepato-renal impairment.

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P35

Geriatric frailty and safety and effectiveness of drug therapy: findings from the systematic literature review

Irena Murínová (1,2), Kateřina Kameníková (1) , Tereza Macháčková (1), Eva Topinková (3) , Daniela Fialová (1, 3)

1 Department of Social and Clinical Pharmacy, Faculty of Pharmacy, Charles University, Czech Republic

2 Department of Clinical Pharmacy, The Millitary University Hospital, Prague

3 Department of Internal Medicine and Geriatrics, 1st Faculty of Medicine, Charles University, Czech Republic

ABSTRACT

Objectives: Principles of how to individualize drug therapy in complex older adults with geriatric frailty are currently intensively studied. The aim of this systematic literature review was to document the current evidence on geriatric frailty and individualization of pharmacotherapy in complex older adults.

Methods: We conducted a systematic literature search in WoS and PubMed databases (2000-2024) using key words "frailty syndrome" (+synonyms) AND "older patients" (+synonyms) AND ("medications" OR "polypharmacy" OR "inappropriate prescribing" OR "deprescribing", including all relevant synonyms)). Only English-language articles and systematic or other literature reviews were selected. The final list of articles was categorized into "general articles" (e.g. on polypharmacy, general medication risks etc.) and "specific articles" (focusing on the risk/benefit of specific drugs/drug classes).

Results: In primary literature search we identified 3 659 studies of those 68 reviews were finally selected, describing: frailty syndrom in general (n= 11), general medication risks (n= 33) and medication-related problems or individualization of drug schemes in specific drugs/drug classes (24 studies), mainly: statins, opioids, antidiabetics, anticoagulants (DOACs), ACEi, betablockers, anticholinergics, β-agonists, α-antagonist and desmopressin.

Conclusion: Limited number of studies is available on efficacy and safety of various classes of psychotropics in older patients with geriatric frailty, while more evidence was published on cardiovascular medications, antidiabetics and anticholinergics. Identification of novel principles of how to individualize pharmacotherapy according to stages of geriatric frailty may lead to novel guidelines for clinical practice and increase in medication safety in complex older patients.

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P36

QUALITY OF LIFE AND FRAILTY SYNDROM IN OLDER PATIENTS: SYSTEMATIC LITERATURE REVIEW

Jitka Pokladnikova[1], Kateřina Kameníková[1], Tereza Macháčková[1], Eva Topinková[2], Irena Murínová[3], Lisa Pont[4], Jindra Reissigova[5], Daniela Fialová*[1,2]

[1]Department of Social and Clinical Pharmacy, Faculty of Pharmacy, Charles University, Czech Republic

[2]Department of Internal Medicine and Geriatrics, 1st Faculty of Medicine, Charles University, Czech Republic,

[3]Department of Clinical Pharmacy, Military Faculty Hospital Prague, Prague, Czech Republic

[4]Graduate School of Health, University of Technology Sydney, Sydney, Australia

[5]Dept of Stat. Modelling, Institute of Computer Science of Czech Academy of Science, Prague, Czech Republic

ABSTRACT

Objectives: The objective of this systematic literature review was to summarize the existing evidence on geriatric frailty and quality of life in older adults in published studies specifically dealing with rational geriatric pharmacotherapy and aspects of frailty.

Methods: A systematic literature search was performed using Web of Science and PubMed (2010–2024), incorporating synonyms for key terms such as "frailty syndrome" AND "aged" AND ("medications" OR "polypharmacy" OR "inappropriate prescribing" OR "deprescribing“) AND “quality of life“. Duplicates and irrelevant articles were excluded through Endnote software and with the use of manual screening of titles and abstracts. Only English-language articles focusing on older adults, medication use, quality of life and relevant study types (e.g., systematic reviews, narrative reviews, scoping reviews, and umbrella reviews) were included.

Results: The final search retrieved 1195 studies, of which 81 articles were systematic literature reviews or other reviews. Further analysis identified 3 systematic reviews focusing on quality of life in older patients and I) evidence in deprescribing interventions, II) anti-hypertensive drugs´ deprescribing and III) the effect of down-titration and discontinuation of heart failure pharmacotherapy.

Conclusion: A wide range of studies has already explored the frailty syndrom and medication use, but already 3 systematic literature reviews specifically studied how deprescribing process or discontinuation of medicines (in general, or in cardiovascular medicines) affects the QoL of older adults. More research is needed about the impact of individualization of drug schemes on physical functioning, independence, psychological well-being and overall QoL in frail older patients.

Disclosure of Interest: None Declared

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