53RD CONFERENCE SYNTHESIS AND ANALYSIS OF DRUGS 2025

September 17-19, 2025 Congress Hotel Kurdějov, Czech Republic

BOOK OF ABSTRACTS

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Synthesis and Analysis of Drugs 2025

We are pleased to invite you to the 53rd conference

SEPTEMBER 17-19, 2025

CONGRESS HOTEL KURDĚJOV, CZECH REPUBLIC

More info on the website SAL 2025

LinkedIn profile of the conference

More information and registration

53rd Conference SYNTHESIS AND ANALYSIS OF DRUGS

The Book of Abstracts

First electronic edition

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ISBN

Content

Welcome Words

Dear colleagues,

On behalf of the organizing committee and Faculty of Pharmacy, Masaryk University, it is with great honor and sincere pleasure that we extend our warmest welcome to you at the 53rd Conference Synthesis and Analysis of Drugs (SAL 2025), held in the picturesque village of Kurdějov, South Moravia.

This conference continues a proud tradition dating back to 1971, bringing together researchers, educators, and professionals from across the Czech Republic, Slovakia, and beyond. We are honored to host this event under the auspices of the Rector of Masaryk University, Prof. MUDr. Martin Bareš, Ph.D., and to provide a platform for the exchange of cutting-edge scientific knowledge in pharmaceutical chemistry, analysis, and related disciplines.

SAL 2025 offers a rich program of lectures and poster sessions, covering topics such as the synthesis and isolation of bioactive compounds, analytical techniques, pharmacology, toxicology, and the structural analysis of natural substances. We believe this diverse and interdisciplinary scope will inspire fruitful discussions and foster new collaborations.

Beyond the scientific content, we hope you will enjoy the unique atmosphere of Kurdějov, known for its hospitality, excellent wine, and scenic surroundings. We encourage you to take advantage of the networking opportunities, engage with fellow participants, and build connections that may last well beyond the conference.

We wish you a stimulating and enjoyable experience at SAL 2025 and a pleasant stay in South Moravia.

Warm regards,

Pavel Bobáľ

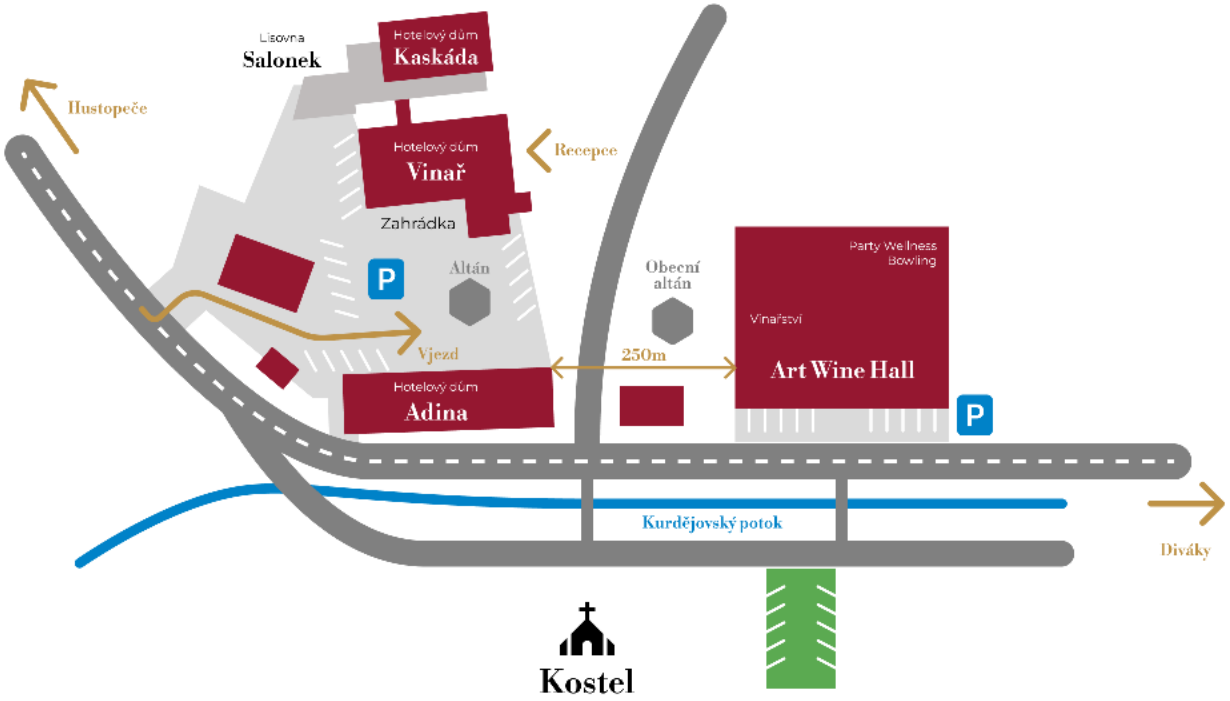
Chair of the Organizing Committee

Venue

Hotel Kurdějov a.s.

Kurdějov 62, 693 01 Kurdějov

Czech Republic



Scientific Committee of the Conference

doc. Ing. Pavel Bobáľ, CSc. (Pharm MUNI) - Chair
Mgr. Michaela Kuchynka Ph.D. (Pharm MUNI) - Co-chair
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Information

Nametags

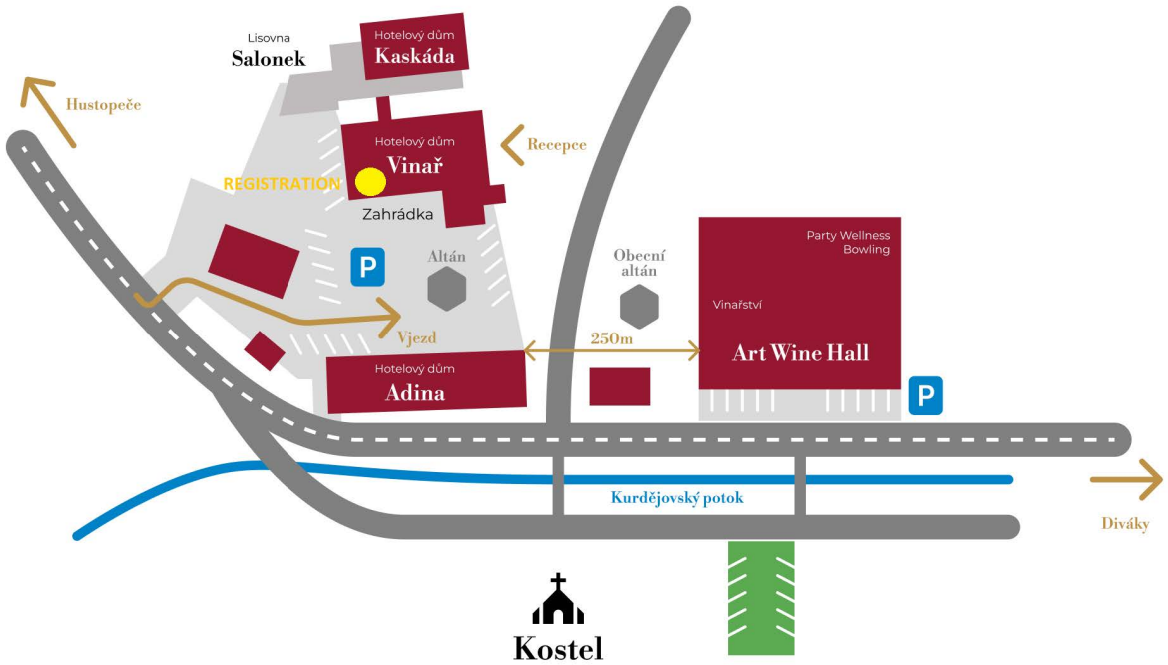
To ensure smooth access throughout the conference, please always keep your nametag visible – this includes meal breaks, social events and evening gatherings. Certain areas and services will require verification.

Lunch Information

Lunch will be provided on the ground floor of the Vinař building, offering a convenient and comfortable setting for attendees to relax and connect between morning and afternoon sessions.

Need Assistance?

Our event organizers will be easy to identify – just look for the black conference badges. If you have any questions or run into any issues, feel free to reach out to them anytime during the conference. Registration to the conference will be held at Vinař building on ground floor.



Poster Session

The poster session is scheduled to be held in Room A1 on the ground floor of the Adina building, running from 15:30 to 17:00.

During the poster session, attendees will showcase their work, with plenty of opportunities for engaging conversations and professional networking. Student submissions will be reviewed by a panel of experts, who will assess each poster for its scientific merit, innovative approach, and clarity of presentation.

Poster Award Committee

Pavel Bobáľ
Norbert Jakubowski
Gunda Köllensperger
Wolfgang Kroutil
Michaela Kuchynka
István Mándity
Viktor Milata
Lucie Nováková
Henrik Sundén
Peter Verwilst

MUNI

AUSPICES OF THE RECTOR OF MASARYK UNIVERSITY

The Rector of Masaryk University, Martin Bareš, grants auspices to the international expertise conference

53rd Conference Synthesis and Analysis of Drugs,

which will be held from 17-19 September 2025 by the Faculty of Pharmacy of Masaryk University in the premises of the Congress Hotel Kurdějov.

I am pleased to accept the patronage of this conference and wish the organisers and all participants a successful event.

MARTIN BAREŠ, THE RECTOR OF MASARYK UNIVERSITY
BRNO 20 MAY 2025

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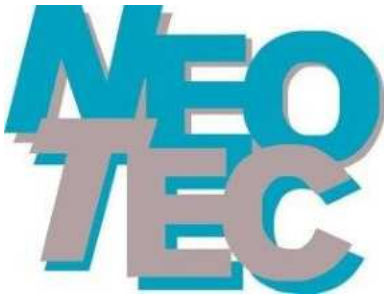

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Seeing beyond

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Conference Program

SAL 2025 – Conference Program

September 17–19, 2025; Congress Hotel Kurdějov

WEDNESDAY – Sept 17

● Conference Day 1 ●

11:00		**Registration & WELCOME COFFEE BREAK** sponsored by STELACHEM spol. s r. o. (Vinař Building, Ground Floor)
13:00		**CONFERENCE OPENING** (Vinař Building, 1st Floor, Room V1)
13:30	**Plenary Lecture**	**David Vetchý** Masaryk University Masaryk University Pharma Park for Industry in Complex
		S1 Labels and Molecular Targets in Drug Research Chair: I. Mándity, co-chair: A. Stehlíková (Rumlerová)
14:00	**Invited Lecture**	**Norbert Jakubowski** Institute for Materials Research and Testing in Berlin Elemental Labels and Tags – Valuable Tools for Drug Development and Application
14:45	Sponsor Talk	Altium International
15:00	**Shor talk**	**E. Havránková** Masaryk University Design, Synthesis and Experimental Validation of Novel Human Carbonic Anhydrase IX Inhibitors
15:15		**K. Bogevski** Goce Delchev University Optimizing Epigallocatechin Gallate Extraction from Biological Sources Using Pectinase: Implications for Oxidative Stress Reduction and Cancer Prevention
15:30		**COFFEE BREAK** (Vinař Building, Ground Floor)
		S2 Synthesis and Design of New Drugs Chair: V. Milata, co-chair: A. A. Needle
16:00	**Invited Lecture**	**István Mándity** Semmelweis University / Research Centre for Natural Sciences Sustainable Flow Chemistry for Peptide Synthesis and Drug Discovery
16:45	Sponsor Talk	ECOM
17:00	**Short Talks**	**P. Dunkel** Semmelweis University One Starting Material – Three Novel Ring Systems
17:15		**J. Otevřel** Masaryk University Asymmetric Organocatalyzed Transfer Hydroxymethylation of Isoindolinones Using Formaldehyde Surrogates
17:30		**M. Kučerová-Chlupáčová** Charles University Boron in Drug Design
17:45		**M. Brázdová** Masaryk University G-Quadruplexes and Their Ligands in Biology of Telomere and Proteins of the P53 Family
18:00	Sponsor Talk	Anton Paar
18:10	Sponsor Talk	Delong Instruments
19:00		**DINNER** (Vinař Building, Ground Floor)
20:00		**Social Evening** (Vinař Building, Ground Floor)
22:00		

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THURSDAY – Sept 18

● Conference Day 2 ●

S3 Advanced Analytical and Bioanalytical Methods I

Chair: N. Jakubowski, co-chair: J. Biskupič

8:30	**Plenary Lecture**	**Lucie Nováková** Charles University Supercritical Fluid Chromatography in Pharmaceutical Analysis
9:00	Sponsor Talk	SIOT Trade
9:15	**Short Talks**	**R. Opatřilová** Masaryk University Anxiolytics as Active Contaminants in Aquatic Environments
9:30		**T. Vaculovič** Masaryk University LA-ICP-MS as an Effective Tool for Studying the Fate of Metals in Organisms
9:45	Industrial Talk	J. Kapitán Palacký University Utilisation of Raman Optical Activity in Drug Analysis
10:00	**COFFEE BREAK** (Vinař Building, Ground Floor)	

S4 (Anticancer) Drug Design

Chair: M. Doležal, co-chair: K. Bogevski

10:30	**Invited Lecture**	**Wolfgang Kroutil** University of Graz Cutting Short the Synthesis of Bioactive Molecules by Using Biocatalysis
11:15	**Short Talks**	**M. Studenovský** Czech Academy of Sciences Polymer Prodrugs of Amines
11:30		**M. Sojka** Czech Academy of Sciences The Toxicity of Mononuclear Piano-Stool Ru(II) Anticancer Agents
11:45	Sponsor Talk	Merck
12:00	**LUNCH** (Vinař Building, Ground Floor)	

S5 Synthetic Strategies and Bioactive Molecules

Chair: W. Kroutil, co-chair: B. Kontra

13:00	**Invited Lecture**	**Henrik Sundén** University of Gothenburg *ortho*-Directed Selective Boron-Based Functionalization Strategies of Aromatic Substances
13:45	**Plenary Lecture**	**Viktor Milata** Slovak University of Technology in Bratislava Synthetic Approaches to the Synthesis of the 4-Quinolone Skeleton
14:15	Sponsor Talk	Phenomenex
14:30	**Short talks**	**J. Chlebek** Charles University Isolation and Purification of Natural Products by Flash Chromatography
14:45		**N. Maafi** Charles University Pilot Exploration of the Aporphine Alkaloid Scaffold for CNS and Infectious Disease Targets
15:00		**M. Bohunčák** Comenius University Bratislava Determination of the Effectiveness of Lotus Extract in Monotherapy and in Combination with Methotrexate on the Activation of the TLR4 Pathway in Adjuvant Arthritis
15:15	**Symposium Photo**	
15:30 – 17:00	**Poster Session & COFFEE BREAK** (Adina Building, Groud Floor, Room A1)	
17:15 – 19:30	**Social Event of Your Choice** (Meet with us at 17:00 – Vinař Building, Ground Floor)	
20:00 – 23:59	**GALA DINNER** sponsored by MIKROCHEM spol. s r. o. (Art Wine Hall Building)	

SAL 2025 – Conference Program

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FRIDAY – Sept 19

● Conference Day 3 ●

S6 Synthetic Strategies in Antimicrobial Drug Discovery

Chair: Henrik Sundén, co-chair: D. Nádaská

9:00	**Plenary Lecture**	**Jakub Švenda** Masaryk University Synthetic Ribosome Inhibitors Inspired by Bactobolin Antibiotics
9:30	Sponsor Talk	BioTech
9:45	**Invited Lecture**	**Peter Verwilst** Catholic University of Leuven Synthetic Strategies and SAR Exploration of 3,4-Dihydroquinazolin-2(1H)-one HIV-1 NNRTIS
10:30		**COFFEE BREAK** (Vinař Building, Ground Floor)

S7 Advanced Analytical and Bioanalytical Methods II

Chair: L. Nováková, co-chair: M. Vlčnovská

11:00	**Invited Lecture**	**Gunda Köllensperger** University of Vienna Enabling Metal Based Drug Research by Single Cell Analysis
11:45	**Short Talks**	**O. Horáček** Charles University Chiral Carboranes as Emerging Pharmacophores: Advances in Enantioselective Separation
12:00		**M. Kuchynka** Masaryk University Correlative Imaging of Ischemic Stroke: Integrating CT and LA-ICP-MS for Next-Generation Theranostic Insights
12:15		**Z. C. Ertekin** Ankara University Quantitative Chemometric Modeling of a Fixed-Dose Antihypertensive Drug Combination
12:30		**J. Pazourek** Masaryk University Rapid Determination of Polyols by HILIC-ELSD
12:45		**J. Jenčo** Charles University Isolation and Determination of Alpha- and Beta-Bitter Acids in Hops and Nutraceuticals
13:00		**CONFERENCE CLOSING** (Vinař Building, 1st Floor, Room V1)
13:30 – 14:30		**LUNCH** (Vinař Building, Ground Floor)

Invited Lectures

Plenary Lectures

Short Talks

Posters

Industrial Talk

Sponsor Talks

Invited Lectures

Dr. rer. nat. Norbert Jakubowski

Institute for Materials Research and Testing (BAM) in Berlin, Germany

Norbert Jakubowski studied physics at the University of Essen/Duisburg and received his PhD at the University of Stuttgart Hohenheim in 1991. He was a senior scientist at the Institute for Applied Spectroscopy (ISAS) in Dortmund (Germany) and head of the division „Inorganic Trace Analysis“ at the Federal Institute for Materials Research and Testing (BAM) in Berlin. He is retired since 2019, but is still active in research and teaching. Presently he is a consultant for the company Spetec GmbH in Erding (Germany). His research interests have been related to elemental mass spectrometry and Analytical Chemistry. He focused on development of instruments and analytical methods for application in the „Life Sciences“. His main research interests for the latter topic have been related to the development of tagging reagents for labelling of antibodies and imaging of nanoparticles and hetero-elements in single cells and tissues to follow the pathway of NP and drugs and to study their interaction with DNA and proteins. He has published more than 240 papers, 3 books and 11 book chapters. He was awarded with some well recognized prizes such as the European Award for Plasma Spectrochemistry or the Ioannes Marcus Marci Medal.

IL01

ELEMENATAL LABELS AND TAGS – VALUABLE TOOLS FOR DRUG DEVELOPMENT AND APPLICATION

N. JAKUBOWSKI [1]

[1] Spetec Gmbh, Am Kletthamer Feld 15, 85435 Erding, Germany; norbi.jakubowski@gmail.com

KEYWORDS: ICP-MS; TAGGING; LABELLING; HPLC; IMAGING

ICP-MS is one of the most sensitive methods in atomic spectroscopy. The sensitivity is directly proportional to the number of atoms in the ion source, an ICP, and thus can be easily calibrated by standards. However, all molecular information is destroyed in the plasma, which makes it less sensitive to matrix effects but also is related to a loss in analytical information of the sample of interest.

In this lecture several techniques will be discussed how to get some molecular information by applying an atomic detector for the detection of molecules and biomarkers by using two important and very versatile tools: labelling and tagging.

The most direct way to provide molecular information in ICP-MS is the application of elements as labels, if they are specific for selected molecules. A label is intrinsically integrated as a part of a molecule and thus does not change the chemistry of the molecule. For instance it is well known from organic mass spectrometry, where for instance enriched isotopes of carbon (^{13}C) are used for labelling of specific molecules used as standard for identification and quantification. Typical elements used in elemental mass spectroscopy are: sulfur (in amino acids or proteins), phosphorus (in ATP, DTP or DNA) or selenium (in amino acids or in seleno-proteins). In all these cases labels are used for quantification and molecular information is provided by coupling of the ICP-MS with separation techniques. In particular chromatographic separations such as GC, LC or HPLC are applied for this purpose. Examples will be given how to determine the phosphorylation status of peptides and proteins and how to study the binding of Cis-Platinum to proteins using gel-electrophoresis for protein separation.

In comparison a tag is artificially binding elements, most often a Rare Earth Element, to organic molecules by a derivatization method to a molecule of interest, which changes the physical and chemical properties significantly. However, depending on the derivatization technique applied it can be designed to bind specifically to (bio-) molecules of interest only. Alternatively it can be used to tag amino-acids, proteins or antibodies. In the latter case it can be used to develop specific immuno-assays for detection of biomarkers in cancer research or to study protein expression. In the first example it will be shown that staining by use of elemental tags provide information about the distribution of DNA and proteins in a single cell imaging experiment studying the uptake of nanoparticles. In the next example a multiplex assay is developed to measure protein expression in toxicology in a protein microarray. In a last example it will be used for detection of cancer-specific biomarkers in biopsy samples of patients.

To summarize: In this lecture different tools will be discussed how to use an ICP-MS for detection of elements used as labels or tags for drug development, cancer research or in toxicology. It will be shown how the sensitivity of an ICP-MS can be improved to reach detection limits at single molecule levels!

Assoc. prof. Dr. István Mándity

Institute of Organic Chemistry, Semmelweis University

Research Centre for Natural Sciences, Hungary

István Mándity is the Head of the Department of Organic Chemistry at Semmelweis University and a senior researcher at the HUN-REN Research Centre for Natural Sciences (RCNS) in Budapest, Hungary. His research focuses on bioinspired peptide-based systems, with particular emphasis on artificial chloride ion transporters and their therapeutic potential in cystic fibrosis, antimicrobial resistance, and oncology. He is also actively involved in the development of sustainable peptide synthesis methods using continuous-flow technologies. Dr. Mándity has received several national and international research grants and maintains close academic and industrial collaborations in the fields of medicinal chemistry, supramolecular chemistry, and drug delivery. He is the author of 75 publications, a co-inventor of 7 patents, and has received 1,417 independent citations. His cumulative impact factor is 278.7.

SUSTAINABLE FLOW CHEMISTRY FOR PEPTIDE SYNTHESIS AND DRUG DISCOVERY

I. M. MÁNDITY [1,2]

[1] Institute of Organic Chemistry, Faculty of Pharmacy, Semmelweis University, 1085 Budapest, Hungary; mandity.istvan@semmelweis.hu; [2] HUN-REN Artificial Transporter Research Group, Institute of Materials and Environmental Chemistry, Research Centre for Natural Sciences, 1117 Budapest, Hungary

KEYWORDS: GREEN CHEMISTRY; CONTINUOUS-FLOW; PROPYLENE CARBONATE; SPPS; PEPTIDE

Peptide synthesis is central to drug discovery and peptide-based therapeutics. While SPPS has advanced significantly since Merrifield's work, it still relies on excess amino acids and toxic solvents like DMF. To address these issues, we developed a scalable and sustainable approach using continuous-flow (CF) technology and propylene carbonate (PC)—a biodegradable, green solvent [1]. By optimizing CF conditions, we reduced amino acid use to 1.5 equivalents, achieving efficient coupling for all 20 proteinogenic amino acids. PC successfully replaced DMF without further optimization, highlighting its suitability as a green SPPS solvent [2]. The method enabled efficient scale-up of complex peptides, including β-peptide foldamers and N-methylated peptides, with high yields and purities. Even difficult or costly sequences were synthesized with minimal waste and reduced solvent use, supporting the integration of green chemistry into industrial peptide manufacturing [3]. The reactor setup is illustrated in Figure 1. The technology has already been applied in peptide-based drug discovery projects.

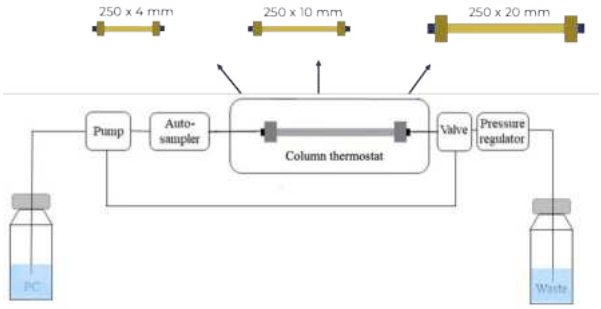

Figure 1. The constructed CF reactor used for SPPS

The study was supported by OTKA ANN 139484, GYORSÍTÓSÁV-2021-00009, TKP2021-EGA-31.

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[2] Mándity, I. M.; Ötvös, S. B.; Fülöp, F. *ChemSusChem* **2014**, *7*, 3172.

[3] Varró, N.; Erdei, E.; Mándityné Huszka, B.; et al. *Chemistry-Methods,* **2025***,* 2500010.

prof. Dr. Wolfgang Kroutil

Department of Chemistry, University of Graz, Austria

Wolfgang Kroutil studied chemistry at the University of Technology in Graz (Austria) and conducted his PhD-research in with Prof. Kurt Faber in Graz at the University of Technology as well as in Exeter (6 months UK, S. M. Roberts). After two years' experience in industry at Novartis/CH and Krems Chemie Chemical Services he became assistant professor at the University of Graz, Austria. After his habilitation he became associate professor in 2004 and full professor in 2013 at the University of Graz (Austria). He published more than 320 papers on biocatalysis and contributed to more than 30 patents concerning biocatalysis. Besides various other awards, he received the Biocat award in 2012 and the Biotrans award in 2015. His research focuses and biocatalytic redox reactions, C-C bond formation and cascades.

CUTTING SHORT THE SYNTHESIS OF BIOACTIVE MOLECULES BY USING BIOCATALYSIS

W. KROUTIL [1], S. VRABL, I. E. E. KROSCHEL, J. SPANG, M. ABRAMIUK, L. GAL, K. GAL, E. LANFRANCHI, F. MASCIA, I. OROZ-GUINEA, J. H. SCHRITTWIESER, C. K. WINKLER

[1] Institut of Chemistry, University of Graz, Austria, Heinrichstrasse 28, Graz, 8042, Austria; Wolfgang.Kroutil@uni-graz.at;

KEYWORDS: BIOCATALYSIS; STEREOSELECTIVITY; C–C BOND FORMATION

Using biocatalysts in organic synthesis is a continuously increasing field. Reasons for that are the mild reaction conditions often using water as solvent as well as the outstanding stereo- and regioselectivity of the catalyst; furthermore, the easy preparation of the catalysts from renewables and the biodegradability of the catalyst represents another aspect of sustainable catalysis. In the lecture examples are given, in which unique features of biocatalysts are exploited and novel/alternative synthetic routes to bioactive molecules are demonstrated.

For instance, an iron-dependent enzyme was shown to catalyze an unprecedent retro-aza-Prins reaction on the route to huperzine alkaloids [1] or we used biocatalysts for stereoselective imine reduction to make (R)-reticuline followed by biocatalytic oxidative C-C bond formation to get (+)-salutaridine [2]. Further examples are the biocatalytic asymmetric Pictet-Spengler reaction of tryptamine and aldehyde enabling a C-C bond formation leading to optically enriched beta-carbolines allowing the shortest synthesis of (R)-harmicine [3,4]. The (formal) reductive amination of ketones enabled e.g. regio- and stereoselective amination of di- and tri-ketones giving access to natural anti-feedant agents [5].

We extended the biocatalytic toolbox e.g. by a biocatalytic Friedel-Crafts like reaction [6], allowing alternative protocols for achieving very recently also C-formylation of catechols (unpublished). Oxidative C-C bond formation in a kinetic resolution gave access to deoxy-, epi-, and podophyllotoxin [7]. Optically enriched acylated 1-indanol, a key intermediate in the synthesis of the blockbuster antiparkinsonian drug rasagiline and the potent neuroprotective agent ladostigil (TV3326) was obtained in a dynamic kinetic resolution using water as solvent and biocatalysts for racemization and acylation, thus metal catalysts could be avoided [8].

The European Community (PharmEco, Marie Curie BioDeCCodiNNg), the Austrian Science Fund (FWF) 10.55776/COE17 for the Cluster of Excellence Circular Bioengineering, the University of Graz, the Doctoral Academy and the Field of Excellence BioHealth are acknowledged for financial support. The COMET center acib: Next Generation Bioproduction is funded by BMK, BMAW, SFG, Standortagentur Tirol, Government of Lower Austria and Vienna Business Agency in the framework of COMET - Competence Centers for Excellent Technologies. The COMET Funding Program is managed by the Austrian Research Promotion Agency FFG.

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[8] A. Rudzka, T. Reiter, W. Kroutil*, P. Borowiecki*, *Angew. Chem. Int. Ed.* **2025**, *64*, e202420133.

prof. Dr. Henrik Sundén

Department of Chemistry and Molecular Biology,

University of Gothenburg, Sweden

Henrik Sundén completed his PhD in Organic Chemistry at Stockholm University in 2007, following undergraduate and licentiate degrees at the same institution. After postdoctoral work in Frankfurt and Gothenburg, he joined Chalmers University of Technology as Assistant Professor, later moving to the University of Gothenburg, where he is currently a Professor. He has been awarded prestigious grants and fellowships, including the ERC MSCA Postdoctoral Fellowships (2018 and 2023), the VR Project Grant (2024), and funding from the Olle Engkvist Foundation (2018 and 2022), among others. He has published over 82 scientific papers, with a total of 5 238 citations and an h-index of 39. Currently, he works in the area of synthetic method development with a focus on boron chemistry—particularly electrophilic ortho diversification—and supramolecular polymer chemistry.

IL04

ORTHO-DIRECTED SELECTIVE BORON-BASED FUNCTIONALIZATION STRATEGIES OF AROMATIC SUBSTANCES

H. SUNDÉN [1],

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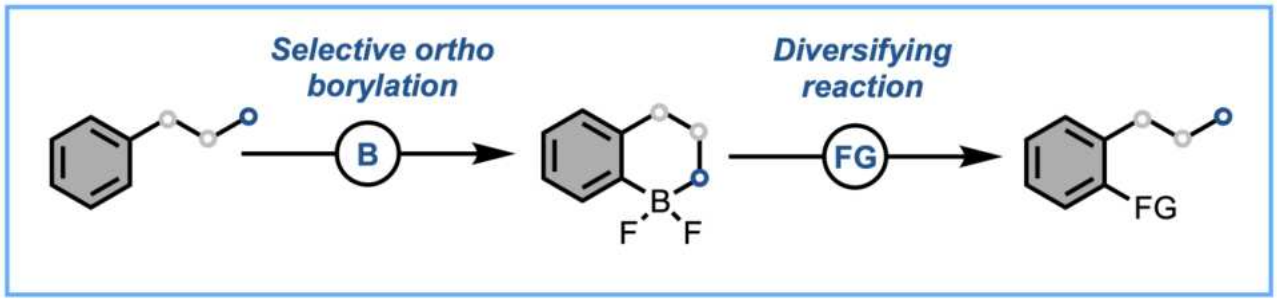
Henrik.sunden@chem.gu.se

KEYWORDS: BORACYCLES; FUNCTIONALIZATION; REGIOSELECTIVITY



A series of highly efficient, regioselective methods for the functionalization of 2-aryl-heteroarenes [1-3] and *N*-aryl amides [4] has been developed, leveraging the unique reactivity of boracycles. These strategies enable installation of diverse functional groups, including halogens (chloro, bromo, iodo), hydroxyl, amine, BF_2, and aryl groups, with exceptional *ortho* site-selectivity and broad substrate scope. Collectively, these methods underscore the synthetic utility of boracycles in enabling precise, diversity oriented, scalable, and operationally simple transformations, with significant applications in medicinal chemistry and materials science.

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Assoc. prof. Dr. Peter Verwilst

Rega Institute, Catholic University of Leuven,

Belgium

Peter Verwilst studied chemistry at KU Leuven (Belgium), completing his PhD research under the supervision of Prof. Wim De Borggraeve and Prof. Wim Dehaen in 2011. He conducted post-doctoral research at Université Bordeaux 1 (France) and served as a Research Professor at Korea University (South Korea) from 2013 to 2019. In 2020, he joined KU Leuven as an Assistant Professor at the Faculty of Pharmaceutical Sciences, with his research lab located within the Rega Institute. In 2025, he became a tenured professor and was promoted to Associate Professor. He has published over 67 papers, resulting in an H-index of 30, and is listed as an inventor on 11 patents. His current research focuses on early-stage synthetic medicinal chemistry, particularly the development of small-molecule antimicrobial drugs and novel allosteric target modulation.

IL05

SYNTHETIC STRATEGIES AND SAR EXPLORATION OF 3,4-DIHYDROQUINAZOLIN-2(1H)-ONE HIV-1 NNRTIS

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KEYWORDS: HIV-1; NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS; 3,4-DIHYDROQUINAZOLIN-2(1H)-ONES; MOLECULAR HYBRIDIZATION

Human immunodeficiency virus type 1 (HIV-1) remains a major global health concern, with the emergence of drug-resistant strains posing a persistent challenge to long-term therapeutic success. Non-nucleoside reverse transcriptase inhibitors (NNRTIs) are a key component of combination antiretroviral therapy, acting through allosteric inhibition of the reverse transcriptase enzyme to suppress viral replication.

We investigated the 3,4-dihydroquinazolin-2(1H)-one scaffold as a novel chemotype for NNRTI development [1]. A modular and efficient synthetic strategy enabled the preparation of a structurally diverse library of analogues, including heterocyclic derivatives of both the *N*1-phenyl substituent and the core scaffold. Structure–activity relationship studies identified multiple compounds with nanomolar potency against wild-type HIV-1. Several analogues also retained activity against clinically relevant resistant strains, including the K103N+Y181C double mutant. Molecular dynamics simulations confirmed the stability of key protein–ligand complexes and revealed favourable hydrogen bonding and hydrophobic interactions.

Our work outlines the synthetic accessibility, structural versatility, and consistent antiviral performance of 3,4-dihydroquinazolin-2(1H)-one-based NNRTIs and heterocyclic core analogues, across a range of viral variants.

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prof. Dr. Gunda Köllensperger

Institute of Analytical Chemistry, University of Vienna, Austria

Gunda Köllensperger is a professor and head of the Department of Analytical Chemistry at the University of Vienna, where she also serves as Vice Dean of the Faculty of Chemistry and Vice President of the Austrian Society of Analytical Chemistry. She studied analytical chemistry at the Vienna University of Technology, where she earned her Dipl. Ing. and Dr. techn. degrees, and later completed her habilitation at BOKU University. She is a recognized expert in mass spectrometry-based methods, multidimensional chromatography, and stable isotope techniques, with over 190 scientific publications. Her research focuses on the development of innovative analytical tools in the fields of metabolomics and metallomics, with a particular emphasis on single-cell analysis and the quantification of trace elements and their chemical species in biological samples. By integrating mass cytometry, her goal is to gain detailed insights into the single-cell ionome in relation to cellular functionality. In collaboration with the Medical University of Vienna, her research group is also involved in the development of targeted anticancer therapies based on metal compounds, particularly platinum complexes, aiming to optimize therapeutic efficacy and minimize side effects.

ENABLING METAL BASED DRUG RESEARCH BY SINGLE CELL ANALYSIS

G. KOELLENSPERGER [1], M. SCHAIER [2], C. MOLITOR, D. LOIBNEGGER, G. BRAUN, L. HENDRIKS

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KEYWORDS: SINGLE-CELL ANALYSIS; LA-ICP-TOF-MS; ELEMENTAL BIOIMAGING; SPATIAL METALLOMICS;

The development of analytical platforms for single cell analysis has transformed our understanding of biological complexity by enabling detailed investigations into cellular heterogeneity and the effects of environmental factors, diseases, and therapeutics on individual cells within tissues. The here presented single cell metal analysis relies on high speed, low-dispersion laser ablation inductively coupled plasma time-of-flight mass spectrometry (LA-ICP-TOF-MS) reaching spatial resolution down to sub-1 µm with ablation rates up to 1000 Hz. Today the platform is at the forefront of elemental bioimaging, referring to the measurement of endogenous and exogenous metal distributions in tissue. The analytical workflow enabling spatial metallomics includes [1] standardization approaches allowing to quantify metal levels at single cell level and [2] a tailored image analysis, for single cell metal quantification based on imaging, scalable to statistically relevant cell numbers and most importantly [3] the full scope of imaging mass cytometry. This way, cellular metal accumulation is linked to phenotypic screening of tissue. We will discuss the impact of the method in the field of metal based anticancer drug development.

Plenary Lectures

prof. Dr. David Vetchý

Department of Pharmaceutical Technology,

Masaryk University in Brno, Czech Republic

David Vetchý is a Full Professor of Pharmaceutical Technology at the Faculty of Pharmacy, Masaryk University. He graduated in Organic Chemistry from the Faculty of Science, Masaryk University, and in Pharmacy from the University of Veterinary and Pharmaceutical Sciences Brno, subsequently specializing in Pharmaceutical Technology. His research focuses on controlled-release dosage forms and advanced drug formulations. Prof. Vetchý served as Head of the Department of Pharmaceutical Technology for 11 years and has been Dean of the Faculty of Pharmacy for the past five years. He has collaborated with both innovative and generic pharmaceutical industries for over two decades. He is the author or co-author of more than 90 scientific publications and holds four patents. His long-term goal is to translate academic research into practical applications that enhance drug delivery and improve patient care.

PL01

MASARYK UNIVERSITY PHARMA PARK FOR INDUSTRY IN COMPLEX

D. VETCHÝ [1]

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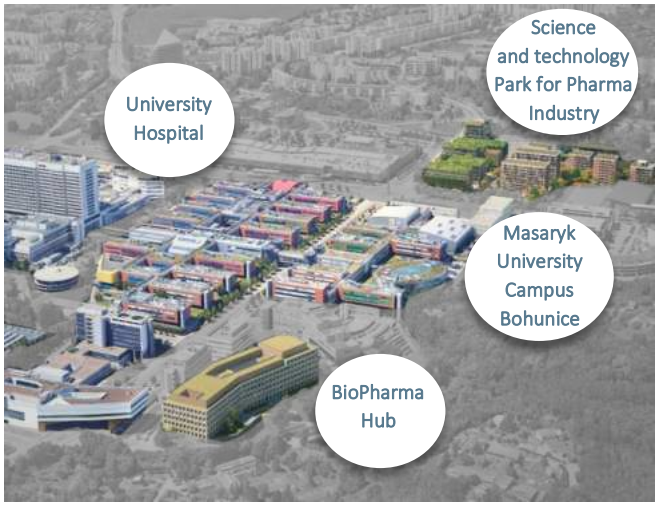
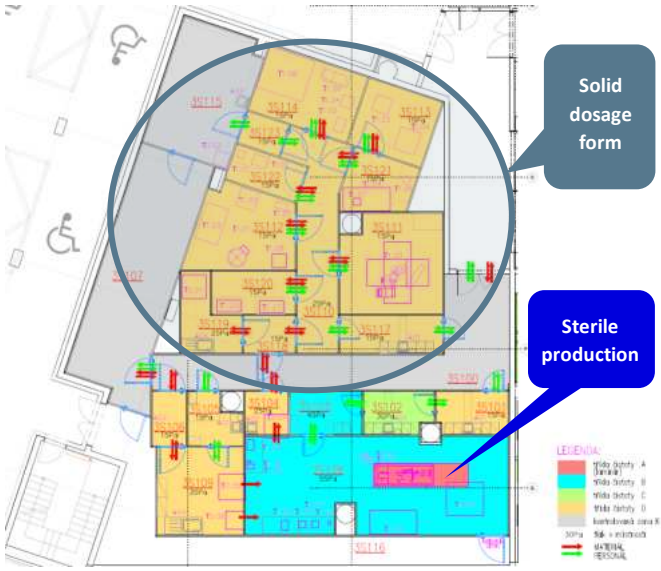
KEYWORDS: PRECLINICAL DEVELOPMENT; GMP PILOT PLAN; CLINICAL TESTING; TECHNOLOGY PARK; PHARMA INDUSTRY

The unique potential of linking pharmaceutical industry research with academia for innovative drug development is built at the campus of Masaryk University in Brno.



In one location will be situated the Faculty of Pharmacy, Faculty of Medicine, Faculty of Science, and the Central European Institute of Technology, with excellent pharmaceutical research. From September 2026, a new infrastructure BioPharma Hub will be open with a state-of-the-art preclinical centre and a completely unique infrastructure for academia, with a GMP pilot plan.



The production unit will include spaces for manufacturing solid dosage forms, sterile aseptic production facilities, and separate parts for physicochemical and microbiological quality control laboratory. Together with the university hospital, it will be possible to ensure the entire drug development cycle from the discovery of the drug substance, through its preclinical testing, preparation of a clinical batch of the dosage form, to the possibility of clinical testing of the drug. In addition, a Science and Technology Park for the pharmaceutical industry will be built nearby to accommodate pharmaceutical companies. All this will create conditions to attract innovative research of pharmaceutical companies to Brno.

prof. Dr. Lucie Nováková

Department of Analytical Chemistry,

Charles University in Hradec Králové, Czech Republic

Lucie Nováková has been a Full Professor in Analytical Chemistry at the Charles University, Faculty of Pharmacy in Hradec Králové, Department of Analytical Chemistry, the Czech Republic since 2019. Her research is oriented towards separation techniques, namely ultra-high performance liquid chromatography, supercritical fluid chromatography, and their coupling to mass spectrometry. She is involved in a broad scope of research projects focused on pharmaceutical analysis, doping control, plant analysis, and bioanalytical methods. An important part of her research also lies in the sample preparation step, where the focus is put on the current trends enabling facilitation, miniaturization, and reduction of time and sample requirements. She authored the book on HPLC theory and practice and ten book chapters. She published almost 180 peer-reviewed scientific articles and review papers with more than 6500 citations and an h-index of 43. She is also widely involved in teaching and education activities, such as HPLC and SFC training courses, seminars, and conferences

PL02

SUPERCRITICAL FLUID CHROMATOGRAPHY IN PHARMACEUTICAL ANALYSIS

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KEYWORDS: SUPERCRITICAL FLUID CHROMATOGRAPHY; API; IMPURITIES; CHIRAL SEPARATION; ACHIRAL SEPARATION

Supercritical fluid chromatography (SFC) combines characteristics of gas and liquid chromatography (LC), employing a supercritical fluid as a mobile phase. Carbon dioxide has been established as the most common SFC mobile phase. As it has non-polar properties, it is often modified with organic modifiers and fine-tuned with additives/s. The low viscosity and high diffusivity of the supercritical mobile phase enhance mass transfer kinetics and reduce pressure drop across the column. Such properties enable high-efficiency separations with shorter analysis times compared to LC. Moreover, reduced organic solvent consumption aligns SFC with the principles of green chemistry.

Pharmaceutical analysis is characterized by rigorous regulatory requirements, adherence to Good Laboratory and Manufacturing Practices, and the necessity to carry out a high number of routine quality control analyses. Initially, only preparative SFC and chiral separations have been used in pharmaceutical industry, as the robustness of the older SFC platforms was not sufficient. Indeed, such methods could not comply with the strict regulatory requirements. Recently, with the introduction of advanced instrumental platforms, SFC has established itself as an important technique in both chiral and achiral workflows.

In achiral applications, SFC enables rapid, high-throughput analysis with complementary selectivity to conventional LC methods, ensuring the effective resolution of active pharmaceutical ingredient (API) from process-related and degradation impurities in line with ICH Q3A/B requirements. This is particularly advantageous for structurally related impurities, where standard LC may lack sufficient resolution. In chiral separations, SFC demonstrates outstanding enantioselectivity, often outperforming conventional HPLC in speed and resolution. Method optimization in SFC might still be challenging. Therefore, efficient screening and optimization workflows have been proposed in both chiral and achiral approaches.

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prof. Dr. Viktor Milata

Institute of Organic Chemistry, Catalysis
and Petrochemistry, Slovak University of Technology,
Slovakia

Viktor Milata focuses on the use of activated double bonds for the synthesis of heterocyclic compounds, particularly 2- and 3-substituted 4-quinolones. He has worked in the chemistry of benzimidazoles, benzotriazoles, benzoselenadiazoles, benzothiadiazoles, quinoxalines, dihydropyridines, and 1,3,5-triazines. He is the co-author of numerous publications, review articles, monographs, and textbooks on NMR and organic chemistry. He is the chairman of the Council of Slovak Scientific Societies at the Slovak Academy of Sciences and honorary chairman of the Slovak Chemical Society. Since 2017, he has been the director of the Institute of Organic Chemistry, Catalysis and Petrochemistry.

PL03

SYNTHETIC APPROACHES TO THE SYNTHESIS OF THE 4-QUINOLONE SKELETON

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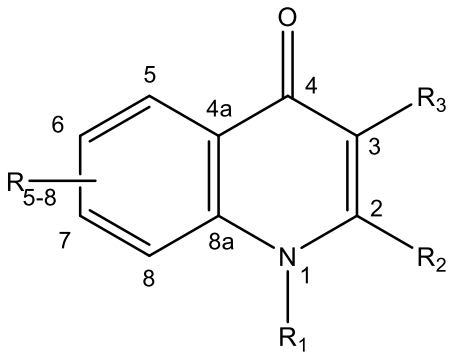
KEYWORDS: 4-OUINOLONES; NAME REACTIONS; BIOLOGICAL ACTIVITY

Compounds with the 4-quinolone skeleton are found in nature and many of them are characterized by a broad spectrum of biological activity [1]. Therefore, the preparation of this type of compounds is a challenge for chemists, especially from a pharmaceutical perspective.



In 2000, we introduced a system for classifying the formation of the 4-quinolone skeleton according to the last bond of the resulting skeleton [2], and this system has been introduced several times, as side chain derivatization is no longer a principle reaction step.

The formation of bonds between C_{8a}-N_1-C_2-C_3-C_4-C_{4a} atoms is the most common, while the generation of a benzene nucleus in the last step is rare [2].

The study was supported by Ministry of education of the Slovak republic, project VEGA 1/0385/25.

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Assoc. prof. Dr. Jakub Švenda

Department of Chemistry, Masaryk University in Brno,

Czech Republic

Jakub Švenda received his master's degree from Masaryk University in 2004. Then, he was the Alfred Bader Fellow in Chemistry at Harvard, working with Professor Andrew G. Myers on the synthesis of DNA-damaging natural products trioxacarcins. After obtaining his PhD in 2010, he returned to Europe. He spent two years as the Humboldt Postdoctoral Fellow at the Max Planck Institute of Molecular Physiology in Dortmund in the team of Professor Herbert Waldmann. Currently, he is an Associate Professor at Masaryk University and a scientist at the International Clinical Research Center of St. Anne's Hospital in the Czech Republic. His research explores strategies and methods to synthesize complex natural products of biomedical relevance efficiently.

PL04

SYNTHETIC RIBOSOME INHIBITORS INSPIRED BY BACTOBOLIN ANTIBIOTICS

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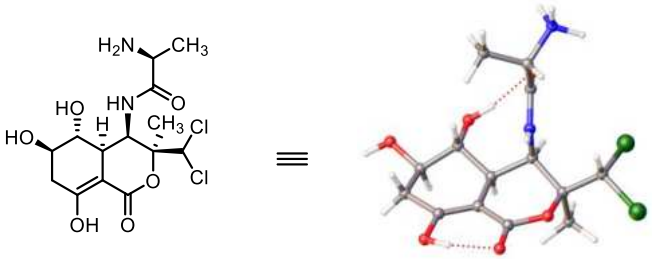
KEYWORDS: ORGANIC SYNTHESIS; NATURAL PRODUCTS; RIBOSOME INHIBITION; ANTIBIOTICS

Bactobolins are complex natural products of polyketide–non-ribosomal peptide biosynthetic origin, which inhibit the growth of gram-positive and gram-negative bacteria. Research has shown that bactobolins work by perturbing protein translation at the ribosomes [1]. In 2015, Ramakrishnan and colleagues revealed how bactobolin A binds to the bacterial ribosome using X-ray crystallography [2]. Bactobolins remain experimental antibiotics however, for they also affect the eukaryotic ribosome. This translates into cytotoxicity and limits the potential use of these natural products in veterinary or human medicine.



(–)-Bactobolin A

Semisynthesis represents the state-of-the-art approach to altering the structure of bactobolins and improving their ribosomal selectivity. Our laboratory is trying to make a meaningful contribution to the problem by pursuing a fully synthetic approach, wherein the modified bactobolins are assembled de novo [3,4]. In this lecture, I will outline the logic of our synthetic plan and highlight key recent developments that resulted in the preparation and testing of unique bactobolin analogs.

The study was supported by the Czech Science Foundation, the Bader Philanthropies, and the National Infrastructure for Chemical Biology CZ-OPENSCREEN.

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Short Talks

DESIGN, SYNTHESIS AND EXPERIMENTAL VALIDATION OF NOVEL HUMAN CARBONIC ANHYDRASE IX INHIBITORS

E. HAVRANKOVA [1], V. VARECKA [2], K. SELIGOVA [1], A. HOFROVA [2], K. RAVASZOVA [2], P. MOKRY [1], M. BITTOVA [2], J. HRITZ [2]

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KEYWORDS: 1,3,5-TRIAZINE; BENZENESULFONAMIDE; CARBONIC ANHYDRASE; ISOZYME SELECTIVITY; STOPPED-FLOW SPECTROPHOTOMETRY

This study presents the design, synthesis and biological evaluation of a new series of 1,3,5-triazinyl benzenesulfonamide derivatives incorporating substituted piperazines, aminobenzenes, or adamantane moieties. The compounds were tested for inhibitory activity against human carbonic anhydrase isoenzymes II and IX, aiming for selectivity towards the latter, cancer associated isoenzyme IX, on the basis of an initial molecular docking screening. Several compounds showed inhibitory activity and selectivity exceeding that of the clinical benchmark acetazolamide and the drug candidate SLC-0111. The compound's inhibition constants were determined using stopped-flow spectrophotometry in an updated approach, which enables accurate K_I determination with higher throughput.

The study was supported by Internal Grant Agency of Masaryk University; Interdisciplinary project number [MUNI/G/1002/2021].

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OPTIMIZING EPIGALLOCATECHIN GALLATE EXTRACTION FROM BIOLOGICAL SOURCES USING PECTINASE: IMPLICATIONS FOR OXIDATIVE STRESS REDUCTION AND CANCER PREVENTION

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KEYWORDS: EPIGALLOCATECHIN GALLATE (EGCG); PECTINASE; ANTISENESCENCE; ANTIOXIDANT ACTIVITY; CANCER PREVENTION

This research focused on developing and optimizing an enzymatic approach for extracting epigallocatechin gallate (EGCG) from Camellia sinensis (L.) leaf material, using pectinase under varying pH, temperature, and solvent conditions. Initial phytochemical screening via UV/VIS spectrophotometry confirmed the presence of catechins, with EGCG as the dominant compound.

Several extraction media were tested, including water, acetate buffer, glycerol, and phosphate buffer. Acetate buffer, while suitable for pectinase activity, caused substantial catechin degradation, indicated by absorbance peaks associated with oxidative byproducts. Glycerol preserved catechin integrity and confirmed the beneficial effect of pectinase but showed limited efficiency. Phosphate buffer emerged as the optimal medium, balancing enzyme activity, catechin stability, and yield.

UV/VIS data confirmed a positive correlation between pectinase concentration and EGCG yield, while literature evidence reinforced EGCG's antioxidant potential through NRF2 and MAPK modulation, NF-κB inhibition, and senescence-related pathways [1].

This work establishes phosphate buffer-assisted, enzyme-based extraction as a promising biotechnological strategy for obtaining EGCG. These findings open avenues for scalable production, formulation improvements (e.g., encapsulation for enhanced bioavailability), and synergistic combinations with other bioactives, supporting the translation of EGCG's effects into nutraceutical and pharmaceutical applications.

References:

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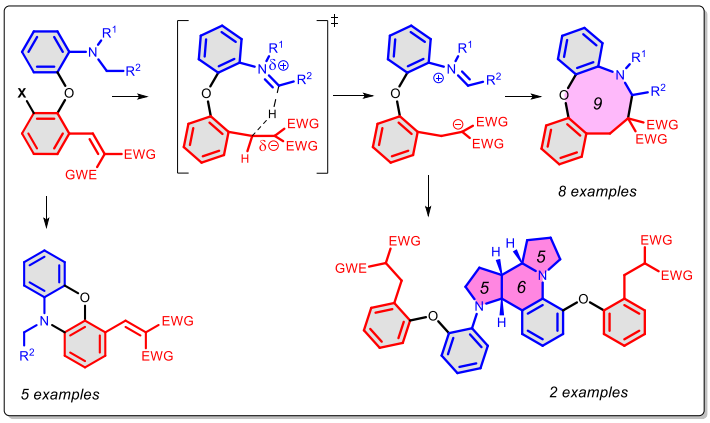
ONE STARTING MATERIAL – THREE NOVEL RING SYSTEMS

P. DUNKEL [1], B. KONTRA [1,2], Z. MUCSI [2]

[1] Institute of Organic Chemistry, Semmelweis University, Hőgyes Endre utca 7, 1092 Budapest, Hungary; dunkel.petra@semmelweis.hu; [2] Department of Biological Chemistry, Brain Vision Center, Liliom utca 43-45, 1094 Budapest, Hungary;

KEYWORDS: HYDRIDE TRANSFER; CYCLIZATION; *N*-HETEROCYCLES

C(sp^3)–H bond functionalizations and C(sp^3)–C(sp^3)-cross coupling reactions are intensively studied transformations, allowing access to complex structures. One type of the C-H bond functionalizations of amines [1], the cyclizations of appropriately substituted tertiary anilines were classified as variants of the '*tert*-amino effect' [2]. A version of these reactions was studied in detail for preparing tetrahydroquinolines. Our aim was to adapt H-transfers/cyclizations to a novel substrate: biaryl ether derivatives.



Although according to computational studies biaryl ethers are less evident substrates for H-transfer/cyclization, the expected oxazonine derivatives were obtained in several cases under thermal conditions. Moreover, during our studies we identified two unexpected cyclization pathways, leading to phenoxazine or octahydrodipyrrolo-quinoline derivatives depending on the substituents [3].

The study was supported by the EKÖP-2024-209 New National Excellence Program of the Ministry for Culture and Innovation from the source of the National Research, Development and Innovation Fund.

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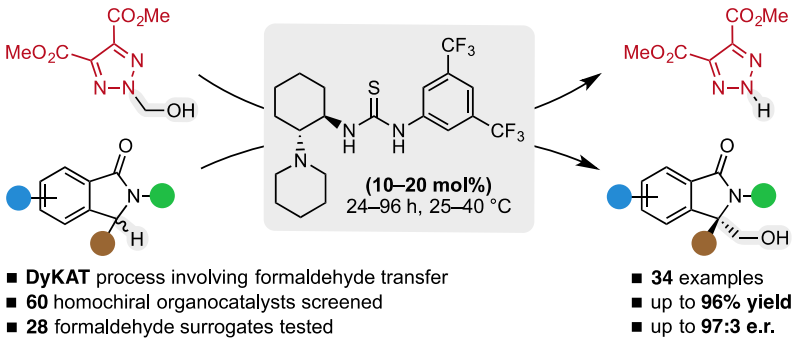
ASYMMETRIC ORGANOCATALYZED TRANSFER HYDROXYMETHYLATION OF ISOINDOLINONES USING FORMALDEHYDE SURROGATES

J. OTEVŘEL [1], D. ŠVESTKA [1], P. BOBÁĽ [1], M. WASER [2]

[1] Department of Chemical Drugs, Faculty of Pharmacy, Masaryk University, Palackého 1946/1, 612 00 Brno, CZ, otevrelj@pharm.muni.cz; [2] Institute of Organic Chemistry, Johannes Kepler University, Altenbergerstrasse 69, 4040 Linz, AT

KEYWORDS: FORMALDEHYDE; ASYMMETRIC ORGANOCATALYSIS; TAKEMOTO CATALYST

The cross-aldol reaction with formaldehyde is a highly efficient method for extending carbon chains that is greatly rewarding in terms of atom economy and increased molecular complexity. Various sources of formaldehyde, such as paraformaldehyde, trioxane, and aqueous formaldehyde, are commonly used for this homologation reaction. Nevertheless, their use has several disadvantages – paraformaldehyde is poorly soluble in organic solvents and has relatively slow chain unzipping, trioxane requires activation with acid, and formalin may cause incompatibilities in catalytic systems owing to the water and methanol presence. Alternatively, anhydrous formaldehyde can be generated in situ from its precursors under the basic conditions [1]. These formaldehyde surrogates have never been systematically investigated and used in enantioselective reactions. To test their superiority over other formaldehyde sources, a challenging asymmetric hydroxymethylation of isoindolinones, which was first reported by Massa *et al*. in 2018, was utterly reoptimized [2]. By employing a combination of the piperidine-based Takemoto-type catalyst and our bench-stable surrogate, we were able to dramatically improve all reaction parameters and expand its scope from 2 to 34 isoindolinone derivatives. A scale-up experiment, enantioselective downstream transformations and preliminary mechanistic elucidations were also carried out [3].



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BORON IN DRUG DESIGN

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KEYWORDS: BORONIC ACID; BENZOXABOROLE; ANTIPROLIFERATIVE; ANTIMYCOBACTERIAL

Boron was somewhat limited in the drug design due to concerns associated with the toxicity of boric acid. Firstly, it was employed in the experimental anticancer therapy, i.e. Boron Neutron Capture Therapy. Since the Millennium began, boron has been used in the drug design of small-molecule drugs, which resulted in the introduction of bortezomib in the therapy of multiple myeloma and some other drugs in other indications. From the chemical point of view, boronic acids, benzoxaborole, and carboranes are the derivatives most often used in clinical practice or drug development [1].

Our lab's contribution is represented by two series. Benzoxaboroles, including heteroarylcarboxamide in the structure, have been screened against a panel of clinically significant fungi and bacteria, including mycobacteria. Cytotoxicity and inhibitory activity against multidrug-resistant clinical isolates of *Mycobacterium tuberculosis* H37Rv have been determined for the most active compounds, which resulted in high selectivity index values [2]. The other synthesised series of boronic acids was based on the similarity with the non-steroidal antiandrogen flutamide. Its aromatic analogues showed higher antiproliferative activity than flutamide, its active metabolite hydroxyflutamide and bicalutamide. The most active compounds had low cytotoxicity in a non-cancerous cell line. The binding mode toward the androgen receptor was explored [3].

Boron offers the option of covalent binding between the potential drug and its molecular targets, and its derivatives are worth further exploration.

The study was supported by the Ministry of Health of the Czech Republic, grant no. NU21-05-00482 and the "COOPERATIO" Program – research area Pharmaceutical Sciences and projects SVV 260 547 and 260 666 (all three from Charles University, Czech Republic).

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ST06

G-QUADRUPLEXES AND THEIR LIGANDS IN BIOLOGY OF TELOMERE AND PROTEINS OF THE P53 FAMILY

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KEYWORDS: G-QUADRUPLEX; TELOMERE; ARMC6; P53 FAMILY

G-quadruplexes in regulatory regions of genes can act as both transcriptional and non-transcriptional modulators. Specific G-quadruplex binding ligands are among potential anti-cancer drugs. In our work, we focused on the ARMC6 protein involved in telomere biology and p53 family proteins in relation to G-quadruplexes as their target binding and regulatory motifs. p53, p63, and p73 can activate and suppress transcription of a wide network of common and unique genes through direct binding to a range of regulatory sites. In addition to responsive elements, p53 has been characterized as a protein that recognizes G-quadruplexes and DNA triplexes [1,2] in the promoter regions of target genes. Large families of proteins containing armadillo repeats (ARMC) play significant roles in cell adhesion, signaling, and cytoskeletal regulation. The ARMC6 protein function remains unclear, with assumed connections to cancer and telomerase activity. We found that ARMC6 binds to G-quadruplexes from the cancer-related promoters (e.g. EGFR, VEGF, and c-MYC) as well as to telomeric RNA repeats. We observed a strong correlation between DNA topology and transcription of p53 and ARMC6 target genes [3]. Various ligands recognizing G-quadruplexes were used to test the effect of the protein-G4 interaction and the regulation of target gene expression in the biology of the p53 family as well as the ARMC6 protein.

The study was supported by the Grant Agency of the Czech Republic, projects no. 19-15168S and 21-28265S.

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ANXIOLYTICS AS ACTIVE CONTAMINANTS IN AQUATIC ENVIRONMENTS

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KEYWORDS: ANXIOLYTICS; BENZODIAZEPINES; CONTAMINANTS; AQUATIC ENVIRONMENTS

Pharmaceuticals, particularly anxiolytics from the benzodiazepine class, represent a specific group of so-called micropollutants with a high potential for sublethal and behavioural effects on aquatic organisms, even at the very low concentrations commonly detected in wastewater and surface waters. These compounds exhibit persistence during conventional municipal wastewater treatment and, due to their biological activity, may affect the neurophysiology and behaviour of non-target aquatic animals, especially fish.

For example, oxazepam has been detected in European rivers at concentrations up to 61 ng/L [1]. Long-term exposure to mixtures of benzodiazepines (temazepam, clobazam, oxazepam, temazepam) has also been shown to result in bioaccumulation in fish tissue and synergistic behavioural effects that cannot be predicted from single-compound exposure [2]. A recent field study [3] investigated the migration behaviour of 279 Atlantic salmon (*Salmo salar*) in the Dalälven River (Sweden), where fish were exposed to an environmentally relevant dose of the anxiolytic clobazam. The results showed that treated individuals migrated faster, exhibited reduced shoaling behaviour, and a greater proportion reached the sea. However, these behavioural changes increased predation risk and disrupted the normal migratory strategy.

In this context, we conducted our own study investigating the prevalence of four benzodiazepines—diazepam and its active metabolites oxazepam, temazepam, and nordazepam—in the waters of two rivers flowing through the second largest city (Brno) in the Czech Republic.

Our findings highlight the need for a revised approach to environmental risk assessment of pharmaceuticals, one that includes behavioural endpoints. The results also support the development of “green pharmacy” principles and technological innovation aimed at improving the removal of these compounds from wastewater.

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LA-ICP-MS AS AN EFFECTIVE TOOL FOR STUDYING THE FATE OF METALS IN ORGANISMS

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KEYWORDS: XENOBIOTICS; LA-ICP-MS; IMAGING

Organisms are exposed to a whole range of xenobiotics, which can enter organisms in various ways. Many of these xenobiotics are metals and their species. Their fate in the organism can thus be monitored using element-sensitive methods. Among the most sensitive is the laser ablation method with inductively coupled plasma mass spectrometry (LA-ICP-MS).

The lecture will present two applications of this technique in monitoring xenobiotics in organisms. The first will be the monitoring of metal nanoparticles that enter the organism through the respiratory system and are transported via the bloodstream to other mouse organs (brain, liver, kidneys, etc.) [1].

The second case focuses on nickel and cells. Nickel is widely used in materials such as joint replacements and is released into the body. The influence of nickel-containing solutions on its uptake into different types of cells and its distribution within the cell will be monitored [2].

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POLYMER PRODRUGS OF AMINES

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KEYWORDS: PRODRUGS; POLYMER; HPMA; CONTROLLED RELEASE

Prodrug strategies represent a powerful approach to optimize pharmacokinetics, reduce toxicity, and enable targeted delivery of therapeutic agents. Among these, reversible derivatization of amine-containing drugs remains a key technique due to the functional versatility of amino groups. While traditional low molecular weight prodrugs often utilize simple functional groups such as esters or carbamates, emerging polymer-based systems offer distinct advantages, particularly in oncology.

This contribution will introduce the rationale behind prodrug design with a focus on amines, and then explore in detail the use of N-(2-hydroxypropyl)methacrylamide (HPMA) copolymer conjugates as advanced macromolecular prodrugs. HPMA copolymers can be engineered to release the parent drug in its active, unmodified form via enzymatically or pH-triggered cleavage in the tumor microenvironment.

Such polymer-drug conjugates maintain the defining feature of prodrugs: inactive or altered form upon administration and in vivo biotransformation to yield the original active compound. The high molecular weight of HPMA systems enables passive tumor targeting via the enhanced permeability and retention (EPR) effect, prolonged circulation times, and improved safety profiles.

This talk aims to highlight how polymer-based carriers—when designed to regenerate the parent amine drug at the site of action—fit within the broader concept of prodrugs, providing a bridge between chemistry and nanomedicine in modern cancer therapy.

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THE TOXICITY OF MONONUCLEAR PIANO-STOOL RU(II) ANTICANCER AGENTS

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KEYWORDS: METALLODRUGS; ANTICANCER AGENTS; SAR;

Half-sandwich complexes of ruthenium resembling a piano-stool shape attract interest as potential anticancer agents [1]. Characterised by significant structural modularity (see Fig. 1) and diverse biological activity [2], these compounds have been in development for more than three decades, resulting in hundreds of compounds. The toxicity of more than 1400 unique compounds (expressed in IC50 values) has been reviewed and will be discussed in depth in the context of a number of tumour and healthy cell lines. The aim is to highlight the relationships between the structure and activity of the complexes and emphasise the importance of specific ligands [3]. The influence of ligand types (e.g., phenanthroline-type bidentate N-donor ligands) on the modulation of the biological activity of the resulting complexes will be highlighted, including the versatility of some ligand combinations. It should be pointed out that the overall picture remains incomplete due to gaps in broader toxicity data collection and the lack of in vivo studies. Some types of cancer are not adequately (or not at all) represented, and the mechanisms of action of Ru(II) cytotoxic agents are not yet fully understood. Despite (or precisely because of) this, future directions of research within the group of Ru(II) complexes will be outlined as a cornerstone addition to the Ru metallodrug field.

Figure 1. The general structure of Ru(II) compounds, showing the ligand arrangement; X, Y, and Z can be mono-, bi-, or tridentate ligands; the π-arene moiety can be a five- or six-membered ring system.

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ISOLATION AND PURIFICATION OF NATURAL PRODUCTS BY FLASH CHROMATOGRAPHY

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KEYWORDS: FLASH CHROMATOGRAPHY; ISOLATION; NATURAL PRODUCTS; DRUG DISCOVERY

Flash chromatography is a rapid, efficient, and cost-effectiveness purification technique, widely used in the separation of synthetic compounds and natural products from plants, fungi, and marine organisms as well, especially in research and development. Modern instrumental flash chromatography systems utilize pressurized solvent flow through a pre-packed cartridges containing mainly silica gel or RP-18 material and ensure rapid separation cycles and ease of use. Thus, Flash chromatography is valuable for isolating target compounds from complex mixtures, including those found in natural sources, enabling researchers to obtain purified compounds for further study [1]. The lecture content is focused on the application of Flash chromatography for the separation and purification of plant secondary metabolites of various structural types, including practical advice, recommendations, and practical demonstrations.

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PILOT EXPLORATION OF THE APORPHINE ALKALOID SCAFFOLD FOR CNS AND INFECTIOUS DISEASE TARGETS

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KEYWORDS: ALKALOIDS; APORPHINE; MYCOBACTERIUM; BUTYRYLCHOLINESTERASE; SEMI-SYNTHESIS

Aporphine alkaloids represent one of the largest subclasses within the structurally diverse group of isoquinoline alkaloids. These compounds occur naturally across numerous plant families and exhibit considerable chemical variation based on the 4*H*-dibenzo[*de*,*g*]quinoline backbone. Even minor modifications to this core structure have led to a wide range of biological activities, highlighting the potential of this scaffold in the treatment of neurodegenerative and metabolic diseases, as well as cancer. A prominent example is (*R*)-(–)-apomorphine, a dopamine D1 and D2 receptor agonist approved by the FDA for the treatment of advanced stages of Parkinson's disease, showcasing the success of aporphine-based scaffolds in drug discovery [1].

While the *R*-aporphine isomers have been extensively studied for their affinity toward dopaminergic, serotonergic, and adrenergic receptors, the *S*-isomers have also attracted attention for their interaction with various central nervous system (CNS) targets, most notably, their inhibitory activity against acetylcholinesterase and butyrylcholinesterase [1].

In this study, (*S*)-(+)-bulbocapnine was employed as a core aporphine scaffold for derivatization and evaluation of its potential in drug discovery targeting CNS-related and infectious diseases. A total of 37 semisynthetic derivatives bearing various substitutions at position 11 and N-6 were synthesized and screened. The results of these evaluations against both CNS targets and pathogens relevant to infectious diseases will be presented.

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DETERMINATION OF THE EFFECTIVENESS OF LOTUS EXTRACT IN MONOTHERAPY AND IN COMBINATION WITH METHOTREXATE ON THE ACTIVATION OF THE TLR4 PATHWAY IN ADJUVANT ARTHRITIS

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KEYWORDS: RHEUMATOID ARTHRITIS; INFLAMMATION; TLR4 PATHWAY; LOTUS EXTRACT

Rheumatoid arthritis (RA) is a chronic disease in which the Toll-like receptor 4 (TLR4) signalling pathway plays a significant role in its pathogenesis [1]. Activation of this pathway leads to the secretion of proinflammatory cytokines, such as IL-1, TNF-α, and IL-6 [2]. Nuciferine, a lotus extract (LE) component, was shown to reduce inflammation in *in vivo* and *in vitro* models [3]. Our aim was to determine the effectiveness of LE in modulating the TLR4 pathway in monotherapy and in combination with methotrexate (MTX) in the adjuvant arthritis (AA) model in Lewis rats.

Arthritic animals were treated with either LE, MTX or their combination. On day 28, all of the rats were sacrificed, and liver tissue samples were collected. Changes in gene expression was evaluated by the qRT-PCR method.

Administering the LE lowered the arthritic score. LE reduced the upregulation of the TLR4 receptor in AA rats in accordance with the recent literature [4]. Moreover, LE modulated mRNA expression of negative regulators of TLR4 (A20, IRAK3, SIGIRR) and IL-10 anti-inflammatory cytokine. The effect of MTX was comparable to that of LE. The effect of MTX on all parameters tested was potentiated by LE. LE alleviated clinical symptoms of AA, and at the transcriptional level, it modulated components of the proinflammatory TLR4 pathway relevant in RA. As LE and MTX were found to interact additively when combined, LE may be beneficial for treating RA. However, further research is necessary.

The study was supported by UK/1033/2025, VEGA 2/0126/23, and VEGA 2/0091/23.

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CHIRAL CARBORANES AS EMERGING PHARMACOPHORES: ADVANCES IN ENANTIOSELECTIVE SEPARATION

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KEYWORDS: CARBORANE; CAPILLARY ELECTROPHORESIS; CHIRALITY; CYCLODEXTRIN; ENANTIOMER

Anionic boron cluster compounds are increasingly gaining attention in medicinal chemistry [1] due to their unique physicochemical and biological properties. Among them, [7,8-nido-$C_2B_9H_{11}$]$^-$ stands out for its improved water solubility compared to *o*-carborane and its role in the synthesis of cobalt bis(dicarbollide)(1-). Despite their inherent at-cage chirality, these anionic compounds are typically used as racemates, and their enantiomer-specific behavior remains largely unexplored.

In our previous work, we demonstrated enantiomeric separation of anionic carboranes using cyclodextrins in HPLC [2]. However, no comprehensive study has addressed the chiral separation of anionic carboranes using capillary electrophoresis (CE) with cyclodextrins. Although some separation of [7,8-nido-$C_2B_9H_{11}$]$^-$ has been reported [3], it required complex capillary coating process, and cobalt bis(dicarbollide)(1-) were separated with low resolution.

This study presents a comprehensive non-aqueous CE method for a chiral separation of [7,8-nido-$C_2B_9H_{11}$]$^-$ and cobalt bis(dicarbollide)(1-) derivatives [4]. Methanolic electrolytes combined with various cyclodextrin derivatives, particularly hydroxypropyl-β-, methyl-β-, and hydroxypropyl-γ-cyclodextrins, proved highly effective as chiral selectors. Our approach employs a bare silica capillary, offering a simple and reproducible approach to chiral separation. Compared to previous methods [3], we achieved superior resolution, peak shape, and efficiency [3].

Notably, we successfully separated seven novel amino-substituted cobalt bis(dicarbollide)(1-) enantiomers using cationic β-cyclodextrin. These findings establish non-aqueous CE as a powerful tool for enantiomeric purity control of chiral at-cage carboranes.

The study was supported by Charles University (SVV 260 666).

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CORRELATIVE IMAGING OF ISCHEMIC STROKE: INTEGRATING CT AND LA-ICP-MS FOR NEXT-GENERATION THERANOSTIC INSIGHTS

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KEYWORDS: BIOIMAGING; THERANOSTICS; LA-ICP-MS; COMPUTED TOMOGRAPHY; STROKE

In recent years, advanced imaging techniques enabling detailed spatial analysis of elemental, metal, and biomolecular distribution in biological tissues have gained increasing relevance [1]. The combination of computed tomography (CT) and laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) offers a novel and complementary analytical platform for pharmaceutical and biomedical research. While CT provides precise anatomical context, LA-ICP-MS delivers highly sensitive elemental mapping and facilitates the monitoring of drug or nanoparticle biodistribution in tissues.

This correlative imaging strategy proves particularly valuable in the development of targeted diagnostic and therapeutic approaches for cerebrovascular diseases, such as ischemic stroke—one of the leading causes of death in developed countries. The integration of data from both imaging modalities allows for more accurate interpretation of biological interactions and significantly enhances our understanding of the mechanisms of action of therapeutic agents or delivery systems in real biological environments.

The combination of CT and LA-ICP-MS thus opens up new possibilities for the development and evaluation of next-generation theranostic tools, with broad applicability in preclinical research and promising potential for clinical translation.

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QUANTITATIVE CHEMOMETRIC MODELING OF A FIXED-DOSE ANTIHYPERTENSIVE DRUG COMBINATION

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KEYWORDS: CHEMOMETRICS; HYDROCHLOROTHIAZIDE; NEBIVOLOL; PHARMACEUTICAL ANALYSIS; UV/VIS SPECTROSCOPY

Nebivolol and hydrochlorothiazide are commonly used as a fixed-dose combination due to their synergistic antihypertensive effects [1]. Accurate and efficient quantification of such combinations in is essential for quality control and regulatory compliance. While chromatographic methods like HPLC are well-established for this aim, they require sophisticated equipment and extended periods of time for separation step. In contrast, direct spectrophotometric techniques offer a faster, cost-effective, and greener alternative, particularly when combined with chemometric models.

In this study, UV-VIS spectroscopic data were collected from 25 binary mixtures of the studied drugs in methanol over the 210–300 nm range with 0.1 nm intervals. Six chemometric regression techniques—Classical Least Squares (CLS), Multiple Linear Regression (MLR), Principal Component Regression (PCR), Partial Least Squares (PLS), Support Vector Machine (SVM), and Artificial Neural Networks (ANN)—were employed to model the data without prior separation. Despite strong spectral overlap, all models demonstrated good performance in calibration step with SVM and ANN showing the lowest prediction errors.

The models were validated on independent synthetic mixtures and applied to commercial tablet samples. Predicted assay values aligned well with label claims. Statistical comparison of ten assay results from per technique using the Kruskal-Wallis test revealed no significant difference ($p=0.05$). However, SVM and MLR showed the lowest prediction bias. ANN, despite excellent calibration results, underperformed in external prediction, likely due to overfitting and the linear nature of the dataset.

These results underscore the feasibility of chemometric models for pharmaceutical analysis, particularly when multiple drugs or interfering species are present in complex formulations.

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RAPID DETERMINATION OF POLYOLS BY HILIC-ELSD

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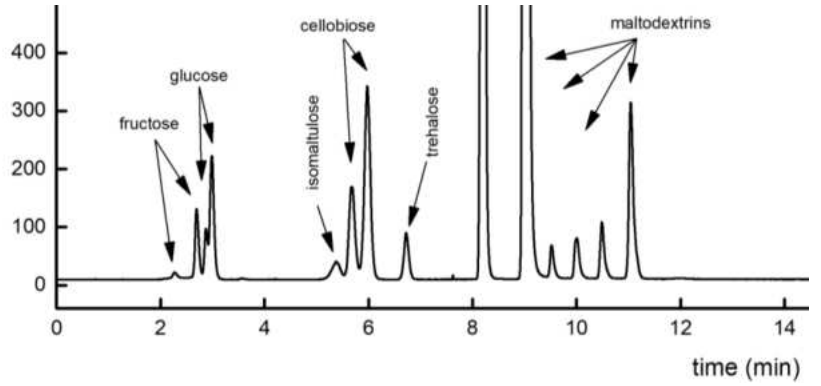
KEYWORDS: ELSD; HILIC; SUGARS; ANOMERS; ISOMALTULOSE

This contribution gives a brief survey of research conducted by the team of the Carbohydrate Separation Group at the Faculty of Pharmacy over the last years. The key separation method was HILIC (Hydrophilic Interaction LIquid Chromatography), a popular tool for separating polar compounds, often without chromophores. A hyphenated detector was the Evaporative Light-Scattering Detector (ELSD), which exhibits many advantages over the Refractive Index Detector (RID) - one is the applicability to gradient elution. Due to the enormous selectivity of diol/pentadiol columns used, it was possible, e.g. to monitor mutarotation anomers [1,2], separate epimers [3], real-time monitor conversion of lactose to lactulose [4] and determine isomaltulose (Palatinose) in food and dietary supplements next to other mono- and disaccharides [5,6]. The primary focus was on separating and determining important saccharides from special nutrition products.



Separation of a carbohydrate mixture. HALO Penta-HILIC (AMT), 35 mM ammonium formate/acetonitrile, 2.0 mL/min, 10 °C, 4 µL.

The study was partially supported by projects MUNI/A/1236/2021 and MUNI/A/1452/2023.

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ISOLATION AND DETERMINATION OF ALPHA- AND BETA-BITTER ACIDS IN HOPS AND NUTRACEUTICALS

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KEYWORDS: HOPS; NUTRACEUTICALS; BEER; CHROMATOGRAPHY; ISOLATION

Humulus lupulus has a long history of being used as a medicinal plant. Numerous phytochemical constituents and secondary metabolites of the hops extract have been studied for their potential therapeutic and cosmetic use. It is most importantly suggested to help alleviate anxiety and insomnia. In Chinese medicine, hops are used to treat insomnia, diarrhoea, and lack of appetite. In addition, alcoholic extracts of the plant have been used to treat tuberculosis, leprosy, and dysentery in the past [1].

In the last decade, a wide range of pharmacological studies have been conducted on the use of individual hop components. These studies were aimed at producing scientific proof of its traditional use. The effects of the plant on the central nervous system have been studied repeatedly in laboratory animals. However, the results of the studies are sometimes contradictory. In vivo studies in rats have shown that the extract of hops containing alpha acids have mainly sedative effects and the beta acids show antidepressant activity [2].

A wide range of nutraceuticals contain hop extract in various amounts. It can also be found in different dosage forms. However, the amount of bitter acids is not mentioned at many descriptions of the supplements. To obtain standards of bitter acids, hop pellets were extracted with the use of LLE, followed by flash chromatography, and preparative LC-MS. Fractions were monitored by HPTLC and GC-MS. To elucidate the concentration of bitter acids a method for the monitoring was developed, optimised, and tested on commercially available nutritional supplements and beer sample.

The study was supported by project SVV 260 662

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Posters

P01

SELECTED PHENYLCARBAMIC ACID DERIVATIVES AND THEIR EFFECT ON BUTYRYLCHOLINESTERASE ACTIVITY

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KEYWORDS: BUTYRYLCHOLINESTERASE; ALZHEIMER´S DISEASE; CARBAMATES; TENSIDE; CRITICAL MICELLE CONCENTRATION; MICELLIZATION

We investigated the effects of selected morpholine ethyl ester derivatives of 2-alkoxyphenylcarbamic acid on the activity of butyrylcholinesterase (BuChE) [1]. Enzyme activity was measured spectrophotometrically at 412 nm according to the Micro-Ellman assay, using DTNB (Sigma) as the thiol reagent and BTCh (Sigma) as the substrate [2]. The percentage of preserved enzymatic activity (*%A*) or inhibition (*%I*) was measured in the presence of the tested compounds within the concentration range of 2.5×10^{-6} to 1.0×10^{-4} mol·L^{-1}. The inhibitory effect and potential were assessed by determining the IC_{50} and pI_{50} values. It was found that an increase in the number of carbon atoms (*n*) in the hydrophobic chain resulted in higher IC_{50} values and a corresponding decrease in pI_{50} values. According to the obtained results, the inhibitory effect increased with a decreasing number of carbon atoms (*n*) in the aliphatic chain, ranging from *n = 9* to *n = 6*. All tested compounds were classified as weak inhibitors of BuChE. A comparison of the calculated *log* IC_{50} and *log CMC* (critical micellar concentration) values revealed that compounds XVI M (*n* = 6) and XIX M (*n* = 7) interacted with BuChE in their monomeric form, whereas compounds XXII M (*n* = 8) and XXV M (*n* = 9) acted in their aggregated form [3]. A linear relationship was observed between *log* IC_{50} and *log CMC*, described by the equation y= –51.43 – 16.24x, with a coefficient of determination $R^2 = 0.97$.

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P02

RATIONAL DESIGN AND *IN-SILICO* STUDIES OF NOVEL POTENTIAL FELINE MCDONOUGH SARCOMA-LIKE TYROSINE KINASE 3 INHIBITORS – ISOSTERIC APPROACH IN STRUCTURE-BASED DRUG DISCOVERY

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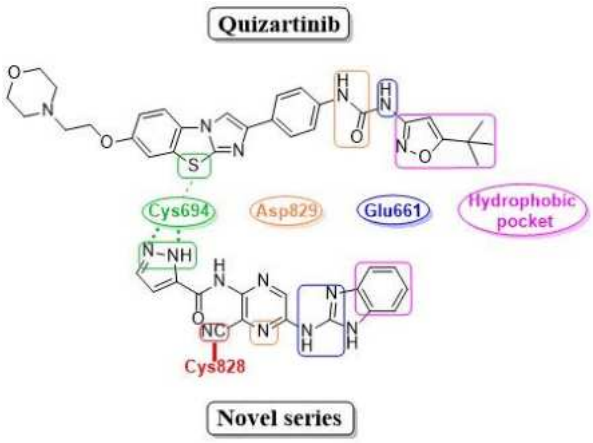
KEYWORDS: ACUTE MYELOID LEUKEMIA; PYRAZINE; TARGETED THERAPY; MOLECULAR DOCKING



Acute Myeloid Leukemia represent only the 1.1% of all cancer diseases in the United States, on the contrary though, has one of the highest estimated mortality rates for the year 2025 [1]. While Feline McDonough Sarcoma-like tyrosine kinase was identified as a primary deregulated target, Quizartinib had been developed to specifically inhibit the inactive conformation of the kinase, nevertheless is facing tolerance due to point mutation in the Kinase Domain and Internal Tandem Duplication mutations [2]. In this study we used an *in-silico* approach to build a novel series with different heterocyclic-based compounds, more likely to form stronger acceptor-donor interaction than Quizartinib with Cys694 in the hinge, while a novelty covalent bond in the region of the pocket where the point mutation occurs has been investigated. Pyrazine-based compounds covalently bound with cyano-moiety, showed an unreported pose in the binding pocket, enhanced by a stabilizing interaction with Asp829. Hence theoretically, the series seems to be unaffected by F691L mutation. MD simulation will be performed to evaluate the stability of the complexes and analyse the binding-unbinding processes, meanwhile the synthesis and the in-vitro testing will serve for biologically validation of the series.

The study was supported by SVV 260666.

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DETECTION OF MICROPLASTICS IN THE BODY: FROM CHEMICAL CHARACTERIZATION TO 3D IMAGING

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KEYWORDS: MICROPLASTICS IMAGING; µCT; LA-ICP-MS; BIOACCUMULATION; ENVIRONMENTAL TOXICOLOGY

The pervasive disposal of plastic waste into the environment presents a substantial challenge for the coming decades, particularly concerning the monitoring and quantification of microplastics (MPs) across various environmental matrices and within living organisms. Despite the recent detection of MPs in a broad spectrum of environmental media and biota, their dispersion mechanisms and toxicological impacts on humans remain inadequately understood [1].

Laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) holds significant promise for identifying polymer alterations [2] and metal markers [3]. However, its direct application in detecting MPs has been limited to tracking trace metals adsorbed on MPs [4]. By enhancing the detectability and imaging of MPs in biological tissues, this research aims to open new pathways for monitoring MPs throughout the human body and assessing potential health effects. Additionally, integrating element-specific imaging from LA-ICP-MS provide the "golden analytical standard" for µCT volumetry to precisely characterize the distribution of MPs within the organ systems. This poster focuses on imaging two sizes of polyethylene terephthalate (PET) MPs, artificially introduced into homogenized rat liver tissue, whole heart, and brain to simulate MPs accumulation.

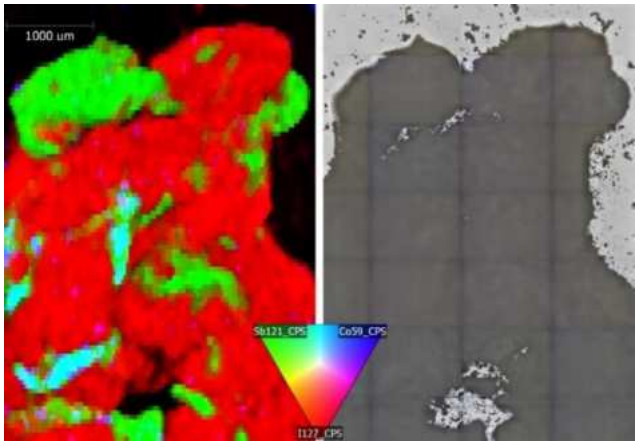

Figure 1: Direct MPs imaging in iodine-stained tissue using LA-ICP-MS

This study was supported by Grant agency of Masaryk University – Specific research, MUNI/A/1450/2024.

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P04

NEW FLUORESCENT MARKERS FOR GLYCAN ANALYSIS

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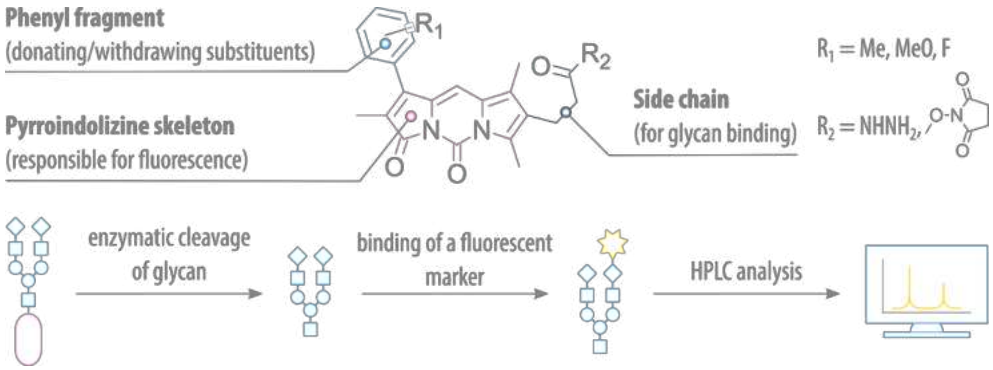
KEYWORDS: FLUOROPHORE; HPLC; GLYCAN

Changes in the composition of glycans correlate with the progression of many diseases, so they are studied as disease markers [1]. However, their analysis is difficult because of the absence of sufficient chromophores. Therefore, they must be labeled with fluorescent molecules [2, 3]. Our goal was to develop a series of new fluorescent markers covalently bound to glycans providing fast labeling kinetics and high quantum yields, allowing glycans to be studied chromatographically (HPLC).

The fluorofor series consists of five molecules differing by substitution on a phenyl fragment (Me, MeO, F). These substitutions will provide molecules with different physicochemical properties. The fluorescent skeleton is based on pyrroindolizine structure. Each fluorophore molecule is prepared in two variants: with a side chain capable of neutral glycan labeling (hydrazide) and aminoglycan labeling (*N*-hydroxysuccinimide ester).

The prepared structures will be characterized in cooperation with the Institute of Analytical Chemistry of the Academy of Sciences of the Czech Republic. The usability of the newly developed fluorophores will be demonstrated by profiling glycoproteins associated with breast cancer.



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P05

AN ALKALOID CENTRIC EXPLORATION OF VINCA MINOR L. AND THEIR BIOLOGICAL ACTIVITIES

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KEYWORDS: VINCA MINOR; ISOLATION; INDOLE ALKALOID; MOLT-4

This study investigates the isolation of indole alkaloids from *Vinca minor* L., and their biological activities related to neuroprotective potential through multi-targeted inhibition relevant to Alzheimer's disease and cytotoxic activity. The alkaloidal extract exhibited notable BuChE inhibition (61.68 ± 4.82% at 2 mg/mL), prompting further fractionation of 90 g of an alkaloidal extract. Five known indole alkaloids (+)-strictamine, (–)-minovincine, (–)-minovincinine, minovincine *N*-oxide, venoterpine, along with one new bisindole alkaloid and one non-alkaloidal compound 3,4dehydrotheaspirone, were isolated using flash chromatography and preparative TLC. Structural elucidation was achieved via MS, NMR, and optical rotation. *In vitro* assays showed weak AChE and BChE inhibition by (+)-strictamine, (–)-minovincine, (–)-minovincinine, and venoterpine (IC_{50} > 100 µM). *In silico* docking studies of (+)-strictamine and (–)-minovincine indicated interactions with TYR, PPAR-γ, and MAO-A through hydrogen bonding, salt bridging, hydrophobic, and van der Waals forces, suggesting potential agonist or antagonist activity. On the other hand, the newly isolated bisindole alkaloid showed significant and selective activity against leukemia cells (MOLT-4) with cell viability 11 ± 4% at 10 µM supporting its further evaluation as a potential anticancer agent.

The study was supported by the specific project of Charles University (No. SVV 260 782).

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P06

HOMODIMERIC BIS-INDOLES POSSESSING ANTIPROLIFERATIVE/CYTOTOXIC ACTIVITY

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KEYWORDS: INDOLE PHYTOALEXINS; BIS-INDOLES; HOMODIMERS; ANTIPROLIFERATIVE ACTIVITY

Indole is one of the most abundant heterocycles in natural and synthetic compounds with medicinal properties. Bis-indole derivatives exert anti-proliferative effects on a wide variety of cancer cells [1]. In this contribution, novel symmetrical bis-indoles containing thiourea/urea moiety **I/II** were synthesized. Cyclization reactions of bis-indole thioureas **I** using various reagents (bromine, methyl bromoacetate) are an effective tool for the preparation of target bis-indole derivatives of 1-methoxyspirobrassinol methyl ether **III** and thiazolidin-4-one **IV**. TFA-promoted cascade rearrangement of spirocyclic bis-indole **IIIa** led to the formation of bis-indole derivative of cyclobrassinin **V**. Bis-indole urea **II** significantly inhibited the proliferation of lung cancer cells A549 with minimal effects on the non-cancer cells [2]. Bis-spiroindole **IIIa** induced apoptosis in colon cancer cells (Caco2, HCT 116) [3].

The study was supported by the Slovak Grant Agency for Science, grant No. VEGA 1/0347/23.

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P07

AMINOPEPTIDASE N: A MOONLIGHTING DRUG TARGET

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KEYWORDS: AMINOPEPTIDASE N; MOONLIGHTING; CANCER; VIRUSES; AADR

The term moonlighting is used for a capability of proteins to have different functions that are not linked one to each other. Aminopeptidase N (APN), E.C. 3.4.11.2, or membrane alanyl aminopeptidase, or CD13 antigen, is a zinc metalloprotease of M1 family. It is virtually omnipresent in the living world. APN exists as membrane-bound (hCD13) or free serum (sCD13) form. As a hydrolase, it inactivates and decomposes various peptides and proteins including neuropeptides and peptide hormones. It is also expressed at the surface of endothelium of cancer vessels. Here, it works as a target for tumour-homing peptides containing NGR (or Asn-Gly-Arg) motif [1]. This motif can be then used for cancer diagnosis, if a fluorescent, a positron-emission tomography (PET) or MRI detectable agent is attached, or a targeted treatment, if a cytostatic agent, or a chelated ("cached") radioactive nuclide is bound [2]. APN serves also as a cell entrance receptor for some coronaviruses and for the human cytomegalovirus (HCMV) [1]. Known APN inhibitors are compounds of both natural and synthetic origin. They have been mainly developed as potential anti-cancer agents. Their cancerostatic effect is attributed to amino acid deprivation response (AADR), also known as cellular starving, caused by inhibition of degradation of proteins including signalling molecules, and subsequent decrease of free amino acids supply in cancer cells [3]. Bestatin, a dipeptide antibiotic from *Streptomyces olivoreticuli,* is used as an adjuvant therapy in acute non-lymphocytic leukaemia in Japan, Korea and China, and is designated as an orphan drug for treatment pulmonary arterial hypertension in the EU. Tosedostat, betulinic acid, psammaplin A and 7-amino-1-bromo-4-phenyl-5,7,8,9-tetrahydrobenzo[7]annulen-6-one are other promising APN inhibitors, and the development continues [4].

The study was supported by the MU Specific Research Grant Project MUNI/A/1496/2024.

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P08

MOLECULAR INSIGHTS INTO THE INHIBITION OF AMYLOID-B AGGREGATION BY NOVEL TETRAHYDROFURAN DERIVATIVES

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KEYWORDS: AMYLOID-BETA; TETRAHYDROFURANS; MOLECULAR DOCKING; MM-GBSA; ALZHEIMER'S DISEASE

We investigated the inhibitory potential of newly synthesized tetrahydrofuran (THF) derivatives on amyloid-β (Aβ) aggregation, a hallmark of Alzheimer's disease (AD). The anti-aggregation activities of the compounds were assessed *in vitro* using the Thioflavin T fluorescence assay, with selected THFs (e.g., W10 and W11) showing low micromolar IC_{50} values. To explore the molecular mechanism of inhibition, we employed molecular docking using the Glide module (Schrödinger Suite) on an *in vitro*-assembled Aβ1-40 fibril structure (PDB ID: 6TI5) [1]. Subsequent pose refinement and binding energy estimation using the MM-GBSA method revealed that the interaction energies did not directly correlate with *in vitro* efficacy. However, visualization of the binding modes indicated a significant distinction: active THFs intercalated between the β-strands of the fibril core, whereas less active compounds remained bound to the fibril surface. This finding suggests that effective inhibitors disrupt fibril elongation by physically inserting themselves into the β-sheet architecture. The docking protocol was further applied to an *in vivo*-derived fibril structure (PDB ID: 6SHS), which displayed markedly different ligand-binding patterns, implying that fibril polymorphism influences ligand recognition. This discrepancy highlights the importance of structural context when translating *in vitro* aggregation assays to *in vivo* efficacy. Our findings provide molecular-level insights into the mechanism of Aβ aggregation inhibition by THFs and emphasize the relevance of the conformational variability of amyloid aggregates in the design of effective therapeutic agents.

The study was supported by the Scientific Grant Agency VEGA 1/0825/25.

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P09

COMPOUNDS ISOLATED FROM A CUBAN ENDEMIC PLANT, *ZANTHOXYLUM FLAVUM* SUBSP. *PISTACIIFOLIUM* (GRISEB). REYNEL, AND THEIR POTENTIAL ANTIMYCOBACTERIAL PROPERTIES.

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KEYWORDS: ZANTHOXYLUM FLAVUM SUBSP. PISTACIIFOLIUM; PREPARATIVE-TLC; Γ-FAGARINE; ANTIMYCOBACTERIAL ACTIVITY;

Zanthoxylum flavum subsp. *pistaciifolium* (Griseb). Reynel is a Cuban endemic plant and is traditionally used to treat ear pain and respiratory ailments [1]. The aim of the study was to isolate compounds from leaves and to evaluate their antimycobacterial activity. Preparative TLC was used for the isolation of compounds and their structures were elucidated by LC-MS, 1D and 2D NMR experiments, and measurements of optical rotation and ECD spectra. The antimycobacterial assay was performed faced five strains of *Mycobacterium* sp. Additionally, a cytotoxicity screening was performed on nine selected human tumor cell lines. A total of six compounds were isolated: three alkaloids, one coumarin, and two glycoside flavonoids. Only compound 2 displayed significant antimycobacterial activity and the other compounds were considered inactive. No significant cytotoxic effects were observed for the tested compounds. This research on the Cuban endemic medicinal plant demonstrates its potential as a source of antimycobacterial bioactive compounds.

The study was supported by from EU-Project "OncoPharm" No. CZ.02.01.01/00/23_021/0008442 and co-funded by Charles University (no. SVV 260 662).

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P10

SEARCHING FOR EFFECTIVE ANTIMICROBIALS: PHENYLCARBAMOYL-NAPHTHYL ALKYL CARBAMATES

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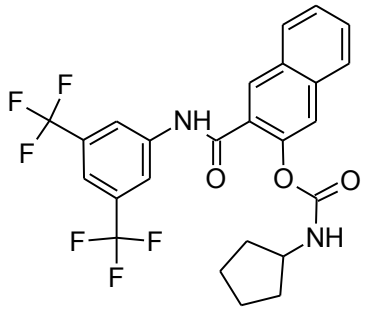
KEYWORDS: ANTIMICROBIAL; MRSA; CARBAMATE; MIC; SYNTHESIS

Recent studies have shown that, despite antibacterial therapy, methicillin-resistant Staphylococcus aureus (MRSA) infections are still associated with serious clinical consequences, especially treatment failure, higher morbidity and mortality, prolonged hospitalization, increased health care costs, etc. Activity against MRSA is of a great importance in the new generation of antibacterial agents because of the worldwide increasing prevalence of this pathogen, more frequent antibiotic resistance to available anti-MRSA drugs, their toxicity and general lack of oral agents [1]. Some recently published derivatives with phenyl-carbamoyl-naphthyl alkyl carbamate moiety have shown excellent antimicrobial activities [2]. The aim of this study was to investigate structure-activity relationships. Series of 70 compounds with different substitution on phenyl ring, position of naphthalene ring and alkyl of carbamate moiety was prepared. Preliminary results of basic antimicrobial screening showed that all compounds were active against MRSA, best of them possess comparable or much better MIC than standards ciprofloxacin and ampicillin. The most active compound is shown on the picture.



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P11

NOVEL FLUORESCENT PROBES BASED ON 2-ARYLPYRIDINE SCAFFOLD AS EFFICIENT GLYCAN LABELS

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KEYWORDS: 2-PHENYLPYRIDINES; SYNTHESIS; FLUORESCENSE; LABELING

Glycoproteins play essential roles in diverse biological processes, including cell signaling, immune response, and disease progression [1–3]. However, their detailed analysis remains a significant challenge due to the structural complexity and typically low abundance of glycans. A major limitation in glycan analysis arises from their intrinsic lack of chromophores or charge, which necessitates chemical derivatization to enable sensitive detection via chromatographic or electrophoretic methods.

To overcome these challenges, we have developed a new class of fluorescent tags based on the 2-arylpyridine scaffold, optimized for efficient glycan labelling through hydrazone-based click-like chemistry. In contrast to conventional BODIPY-derived fluorophores, which in our previous work proved synthetically demanding, involving multi-step procedures and labor-intensive purification, our 2-arylpyridine-based probes offer straightforward synthesis, excellent solubility in polar solvents, and broad chemical versatility, making them highly practical and accessible alternatives. [4]

This work focuses on the design, synthesis, and derivatization strategies employed to prepare several representative 2-arylpyridine derivatives, their transformation into hydrazide-functionalized probes, and the key synthetic challenges encountered along the way, demonstrating the versatility and practical applicability of the scaffold.

This work was supported by the Grant Agency of the Czech Republic [22-00236S].

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P12

DEVELOPMENT OF A BIORELEVANT DISSOLUTION METHOD FOR SIMULATING THE GASTROINTESTINAL TRACT OF BROILER CHICKENS

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KEYWORDS: BIORELEVANT DISSOLUTION TEST; MONOBUTYRIN; *IN VITRO* DIGESTION; FUNCTIONAL FEE; BROILER CHICKEN

Dissolution testing is a crucial (*in vitro*) tool for evaluating controlled-release formulations of active substances, as it enables the quantification of the rate and extent of active substance release under conditions simulating the gastrointestinal tract. However, standard (pharmacopeial) methods often fail to adequately reflect physiological conditions, which can lead to inaccurate predictions of active substance absorption.

This research focused on developing a biorelevant dissolution methodology and testing two distinct formulations – hydrophobic powder and pellets. Special attention was given to the monobutyrin, a butyric acid derivate known to improve gut health and performance in poultry [1]. For the experiment were created simulated gastric and intestinal fluids, incorporating enzymatic activity, the presence of bile acids, and a pH gradient. Experiments were conducted using both standard pharmacopoeial apparatus and the Golem v2 device, which enables advanced simulation of gastrointestinal conditions.

The results revealed differences in the dissolution profiles of the two formulations, contributing to a better understanding of active substance release mechanisms and the optimization of its efficacy. This approach may lead to more accurate *in vivo* predictions of active substance behavior and a reduced need for costly pharmacokinetic studies.

The study was supported by MUNI/A/1445/2023 and QL24010284

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DEVELOPMENT OF NOVEL FLUOROPHORE DERIVATIVES FOR GLYCAN ANALYSIS

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KEY WORDS: BODIPY; FLUORESCENT TAGS; GLYCAN ANALYSIS; HYDRAZONE

Protein glycosylation and the impact of glycan structures on their function represent a crucial area of research in disease diagnostics and the analysis of pathogenic mechanisms. However, glycan analysis is challenging due to their structural variability and the limited sensitivity of existing analytical methods. Therefore, a combination of fluorescence detection and mass spectrometry (MS) is often employed [1].

We focused on the development of novel fluorophore derivatives containing sulfonic and cationic groups, enhancing their solubility in aqueous solutions and improving glycan detection sensitivity. These modifications are based on established skeletal structures such as BODIPY. Additionally, a hydrazine moiety is incorporated to facilitate stable binding with oligosaccharides through hydrazone chemistry.

This approach offers higher reactivity with carbonyl-containing carbohydrate compounds, ensuring the formation of stable complexes suitable for fluorescence detection and MS analysis. The hydrazine-functionalized fluorophores are synthesized via "click" chemistry to ensure compatibility and synthetic efficiency.

The developed labeling methods provide an innovative approach for more sensitive and accurate glycan analysis, contributing to a better understanding of biological processes and disease diagnostics.

The study was supported by project MUNI/A/1404/2023

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P14

ASSESSMENT OF LIPOPHILICITY OF POTENTIAL JANUS KINASE INHIBITORS USING REVERSED-PHASE HPLC AND COMPUTATIONAL PREDICTORS

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KEYWORDS: LIPOPHILICITY; RP-HPLC; COMPUTATIONAL PREDICTORS; JANUS KINASE INHIBITORS

A series of 10 potential Janus kinase inhibitors used in cancer and inflammatory diseases treatment was synthesized. The lipophilicity of newly synthesized substances was assessed using the RP-HPLC method and computed via several interactive tools (MLOGP, CLOGP 4.0, WLOGP, ALOGPS, XLOGP3, and miLogP 2.2). Chromatographic measurements were performed on a Dionex UltiMate 3000 Series UHPLC System using a Symmetry® C18 5 µm, 4,6 x 250 mm column. 10 µL of a methanolic solution of the substance with an approximate concentration of 0,01 mg/mL was injected. The flow rate of the mobile phase was 1 mL/min. The column temperature was maintained at 40 °C. A wavelength close to the absorption maximum of the studied substances (260 nm) was chosen for detection. The analysis was performed in six methanol/water mobile phases with volume ratios of 90:10, 85:15, 80:20, 75:25, 70:30, 65:35 (*V*/*V*). The measurement of each substance in each mobile phase was performed three times. Methanolic solution of potassium iodide was a dead time marker. Based on the retention times of studied substances (t_R) and dead time (t_0), the logarithms of the capacity factors $\log k = \log((t_R - t_0)/t_0)$ were calculated. The linear dependence of the $\log k$ values on the methanol content in the mobile phase was extrapolated to zero methanol content in the mobile phase. Thus, the $\log k_w$ value was obtained, which is used as a lipophilicity parameter corresponding to the aqueous environment. Furthermore, all the experimentally determined $\log k_w$ values were correlated with the *in silico* generated logarithmic values of partition coefficients ($\log P$) for an octan-1-ol/water partition system, and the relationship between lipophilicity and structure of the studied substances was evaluated.

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

DEVELOPMENT AND MECHANISTIC STUDIES OF QUINOLINE PHOTOCAGES FOR BIOLOGICAL APPLICATIONS

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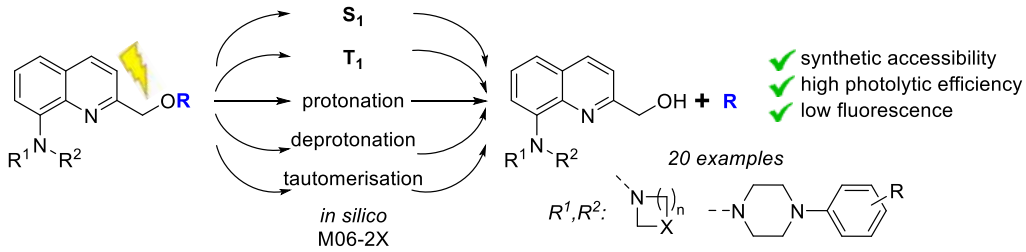
KEYWORDS: DRUG DELIVERY SYSTEMS, QUINOLINE PHOTOCAGES, TWO-PHOTON UNCAGING

Photocages (PPGs) allow the temporally and spatially selective release of biologically active agents, exploiting a light stimulus for the cleavage of a covalent bond between the protecting group and the attached substrate [1]. Beyond the first described neuroscientific applications, photocages can serve as a drug-delivery system for different small molecule drugs [2].



We aimed to prepare and characterize novel 8-aminoquinoline derivatives [3], choosing the 8-dimethylaminoquinoline photocage as our starting point. We wished to implement a simple and robust synthetic pathway and study the effect of modifications in position 8 on the photophysical and photochemical properties. To better understand the structure-property relationships and to guide future PPG design, we set out to study the uncaging process by computational chemistry.

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P16

4-AMINOBENZOIC ACID-BASED IMINES AS POTENTIAL ANTIFUNGAL AGENTS

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KEYWORDS: 4-AMINOBENZOIC ACID; ANTIFUNGAL ACTIVITY; IMINES; SYNTHESIS

The alarming rise in fungal infections and growing resistance to existing drugs represents a significant healthcare challenge and underscore the urgent need for more effective therapies [1]. 4-Aminobenzoic acid (PABA), while non-essential in humans, plays a crucial role in folate biosynthesis in many pathogens. PABA analogues have exhibited notable antimicrobial effects, including resistant strains. 3,5-Dihalogenosalicylaldehydes were found to be optimal for modifying PABA. Thus, PABA-based imines offer a promising strategy, offering a simple scaffold that enables tuning of biological activity [2,3].

In this study, we studied 26 new analogues of methyl (*E*)-4-[(2-hydroxy-3,5-diiodobenzylidene)amino]benzoate, modifying carboxylic group (esters, amides), aromatic rings, positional isomerism, reduction of double bond, and linker length between substructural motifs, etc.

The compounds were evaluated for antimycobacterial, antibacterial, and antifungal activities. They exhibited excellent antifungal activity against both yeasts and moulds including clinical isolates (MIC ≥1.56 μM), modest inhibition of G+ bacteria and minimal antimycobacterial action. The most active derivatives underwent further studies of antifungal action (time-kill assay, determination of type of action, checkerboard assays with established drugs). Notably, they also lack haemolytic properties and *in vivo* toxicity, supporting their potential as safe and effective antifungal agents.

The study was supported by Ministry of Health of the Czech Republic, grant nr. NW24-05-00539 and by the project National Institute of Virology and Bacteriology (Programme EXCELES, ID Project No. LX22NPO5103) – Funded by the European Union – Next Generation EU.

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P17

COMPOUNDS WITH POTENTIAL ACETYLCHOLINESTERASE INHIBITORY ACTIVITY

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KEYWORDS: ACETYLCHOLINESTERASE INHIBITORS; MANNICH SYNTHESIS; CARBAMATES

Acetylcholinesterase inhibitors still play important role in Alzheimer‘s disease therapy [1]. Various compounds were prepared based on the structure of the compound (Fig. 1) with promising inhibitory activity [2]. The lecture briefly reviews the synthetic pathways of the prepared compounds and the effect of particular structural changes on their inhibitory activity.

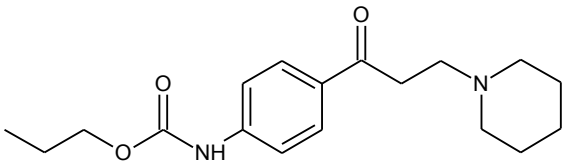

Fig. 1 – Structure of the originally prepared and studied compound.

The structural changes include the amine part of the molecule, where were used some cyclic amines of different ring sizes. Substituents position and additional substitution on the benzene ring was also studied. Slightly more substantial change is using of urea functional group instead of the carbamate. The most substantial change was inserting an amide group instead of the ketone.

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P18

NOVEL PHENYLPYRIDINE-BASED TAGS FOR *N*-LINKED GLYCAN PROFILING BY CE/LED-IF OR CE-MS ANALYSIS

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KEYWORDS: GLYCAN; LABELING; PHENYLPYRIDINE; CAPILLARY ELECTROPHORESIS

Glycosylation analysis is challenging due to the structural complexity and varied conjugation patterns of glycans, along with technical limitations like detection sensitivity. Therefore, a derivatization step is always required before analysis, especially by electrophoretic separation methods with fluorescence or mass spectrometric detection. This study introduces novel labeling reagents based on phenylpyridine with a hydrazide functional group, designed for glycan profiling using CE/LED-IF and/or CE-MS. The newly designed and synthesized hydrazide derivatives, 6-[4-(dimethylamino)phenyl]pyridine-3-carbohydrazide and 6-[4-(4-methylpiperazin-1-yl)phenyl]pyridine-3-carbohydrazide, were characterized using various analytical techniques, including NMR spectroscopy, fluorescence spectroscopy, and MS. The hydrazide group enables efficient labeling via hydrazone formation chemistry, eliminating the need for a reduction step. The positive charge of the tags makes them ideal for both electrophoretic separation and MS detection in positive ion mode. With fluorescence excitation maxima in the range of 300-400 nm, these labels are well-suited also for LIF/LED-IF detection using commercially available solid-state laser or light-emitting diode sources, enhancing detection sensitivity and quantitation limits. Electrophoretic analysis in a neutral-coated capillary achieved baseline separation of labeled oligosaccharides, with detection limits in the nanomolar (MS) or picomolar (LED-IF) range. The optimized labeling and separation conditions have been successfully applied to N-linked glycan profiling of various glycoproteins, including therapeutic monoclonal antibodies.

The study was supported by the Ministry of Education, Youth and Sports of the Czech Republic (9F23002) and the institutional research plan (RVO:68081715). This research was co-funded by the European Union under the ATEBIO project (Advanced Techniques for Biomedical Diagnostics, Project ID CZ.02.01.01/00/23_020/0008535).

P19

SYNTHESIS OF GOLD NANOPARTICLES USING NATURAL COMPOUNDS AS REDUCTING AGENTS

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KEYWORDS: ARBUTIN; LICHEN ACIDS; NORBADION A; PARTICLE SIZE; POLYPHENOLS

Gold nanoparticles have numerous biological effects (antineoplastic, antibacterial, antiphlogistic, and many others) or can be used as carrier systems for drug transport. Gold nanoparticles are prepared using various reducing agents such as: sodium citrate, ascorbic acid, plant extracts or sodium borohydride [1]. The stability of the prepared nanoparticles depends on the used reducing agent. If sodium borohydride is used, a stabilizer needs to be added to increase the stability of the nanodispersion. Surfactants are often used for this purpose [2]. In the case of using natural compounds/extracts, they act as both a reducing agent and a stabilizer [1].

The aim of our work was to study the effect of natural compounds on the stability of prepared gold nanoparticles. The natural compounds were arbutin, evernic acid and norbadione A. All compounds are polyphenols. Arbutin was commercially obtained and it is a glycosylated hydroquinone found in *Arctostaphylos uva-ursi* (bearberry). Evernic acid was obtained from the lichen *Evernia prunastri* (oakmoss). Norbadione A was isolated from the fungus *Pisolithus arrhizus* (deyball). All compounds used were able to reduce tetrachloroauric acid to colloidal gold. The nanodispersions were characterized by UV-VIS spectroscopy, dynamic light scattering and zeta potential. The properties of the prepared nanoparticles were compared with nanoparticles prepared by the Turkevich method.

The study was supported by grant APVV-23-0349 "Optimized composite gold and silver nanoparticles for biomedical applications"

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P20

NOVEL ARYLOXYAMINOPROPANOLS CONTAINING AN ELONGATED SALT-FORMING MOIETY AS PROMISING ANTIMYCOBACTERIALS

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KEYWORDS: ARYLOXYAMINOPROPANOLS; ANTIMYCOBACTERIAL AGENTS; DRUG-LIKENESS

Tuberculosis (TB) remains a long-standing very serious global health threat, as an estimated one fourth of the world's population is infected with *Mycobacterium tuberculosis* and 5–10% of those infected develop TB during their lifetime [1, 2]. The design and development of new therapeutic agents, the optimisation of the dose of clinically approved drugs, and introduction of repurposed drugs have raised hopes for further improvement in the safety and effectiveness of particular regimens [3]. Several precisely designed compounds consisting of a bulky lipophilic moiety (naphthalen-1-yl(phenyl), or a mono- / disubstituted quinolin-3-yl fragment could be present, for example), polar etheric bridge, 2-hydroxypropan-1,3-diyl linker, and moiety with a protonizable atom(s) very effectively fought *in vitro* a drug-sensitive *M. tuberculosis* $H_{37}R_v$ [4, 5]. Their lipophilic fragments, and electrostatic interactions formed between these ligands and a binding site of ATP synthase present in a given mycobacterial strain were decisive factors for such a type of pharmacological activity. Therefore, current research focused on the *in vitro* screening of synthesized *N*-{2-[4-(aminosulfonyl)-/ 4-(fluoro)phenyl]ethyl}--2-hydroxy-3-{4-[(alkoxycarbonyl)amino]phenoxy}propan-1-ammoniun chlorides (alkoxy = methoxy to propoxy) against *M. tuberculosis* $H_{37}R_v$, *M. avium* My. 330/88, *M. kansasii* My. 235/80, and *M. kansasii* My. 6509/96 (clinical isolate) as well as *in silico* evaluation of some of the structural, and physicochemical parameters of these compounds that contributed to their drug-likeness.

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

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P21

SYNTHESIS OF NEW 1,3,4-THIADIAZOLE DERIVATIVES WITH POTENTIAL ANTIMICROBIAL ACTIVITY

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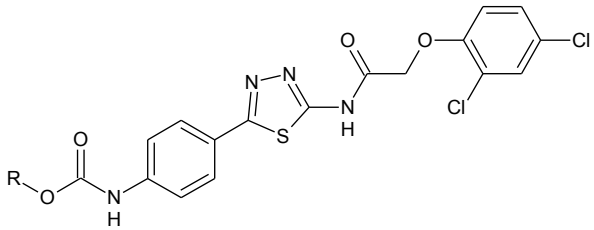
KEYWORDS: 1,3,4-THIADIAZOL-2-AMINE; CARBAMATE; SYNTHESIS; ANTIBACTERIAL ACTIVITY; ANTIFUNGAL EFFECT

Derivatives of (thio)semicarbazides and their increasingly studied cyclic thiadiazole analogues represent promising scaffolds for the development of novel antimicrobial agents. Among them, 1,3,4-thiadiazol-2-amine derivatives are particularly notable for their broad spectrum of biological activities, including antibacterial, antitubercular, and antifungal effects [1]. In this study, a five-step synthetic route was employed to prepare a series of 1,3,4-thiadiazol-2-amine derivatives, with a 4-aminobenzoic acid as the starting molecule. In the first step of the synthesis, carbamate groups with different alkyl chain lengths were incorporated into the reactant structure, followed by the conversion of carboxylic acids into more reactive acyl chlorides. These intermediates then reacted with thiosemicarbazide to yield the corresponding acyl thiosemicarbazides. Subsequently, the corresponding derivatives of 1,3,4-thidiazol-2-amine were prepared by acid-catalyzed cyclodehydration. In the final step, a 2,4-dichlorophenol moiety was introduced via two different synthetic approaches. Reaction progress and compound purity were monitored by thin-layer chromatography (TLC), and the structures of all newly synthesized compounds were confirmed by NMR and IR spectroscopy. All 16 newly prepared derivatives were subjected to preliminary antimicrobial screening against reference strains *Escherichia coli*, *Staphylococcus aureus*, and *Candida albicans*. The results revealed mild to moderate growth inhibitory activity across the tested microorganisms.



General structure of the prepared 1,3,4-thiadiazole derivatives

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P22

SYNTHESIS AND EVALUATION OF AMINOACETOPHENONE-DERIVED KETIMINES AS POTENTIAL THERAPEUTIC AGENTS

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KEYWORDS: SCHIFF BASES; BASIC ACETOPHENONE DERIVATIVE; METALLOENZYME INHIBITOR

Schiff bases are versatile ligands widely used in metal coordination chemistry, capable of forming stable complexes with a broad range of metal ions. These complexes exhibit extensive therapeutic potential, including antibacterial, antifungal, antiviral, antimalarial, anti-inflammatory, cytotoxic, enzyme-inhibitory, and anticancer properties [1]. Due to their ability to form such complexes, many Schiff bases also serve as important intermediates in various enzymatic reactions. One potential target enzyme is aminopeptidase N (AP-N), a neutral zinc-binding metalloenzyme. Inhibitors of this ubiquitous enzyme may offer broad-spectrum therapeutic applications. Both AP-N and the nuclear factor kappa-B (NF-κB) are critical components involved in various cellular processes. AP-N, which plays a role in peptide metabolism, and NF-κB, a key transcription factor in inflammatory pathways, appear to be functionally connected in the regulation of inflammation and immune response. AP-N may influence NF-κB activation through the metabolism of peptides involved in inflammatory pathways. These two factors may also cooperate in the context of cancer biology and metastasis [2].

The series of basic thiosemicarbazone, semicarbazone, and hydroxylamine derivatives of acetophenone with diverse substitution of various symmetrical secondary amines and heterocyclic amines, were synthesized. Compounds showing the most potent inhibitory activity against AP-N (based on IC_{50} values) were further tested for their ability to inhibit cell proliferation in three different cell lines. These lead compounds are now also being tested for their potential to inhibit the pro-inflammatory transcription factor NF-κB, in an effort to uncover deeper connections between AP-N inhibition and inflammation-related signaling pathways.

The study was supported by the project MUNI/A/1496/2024.

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P23

SOLID PHASE CHANGES OF WARFARIN IN TABLETS

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KEYWORDS: GENERIC SUBSTITUTION; BIOAVAILABILITY; STABILITY; SOLID-STATE NMR

Warfarin is still a massively prescribed anticoagulant, especially in the US and for elderly patients [1]. Warfarin is available as warfarin sodium in drug formulations because of its physicochemical properties, especially solubility, that are considerably better than those of its acidic form. Additionally, warfarin sodium exists in amorphous and crystalline forms. The content of the amorphous or crystalline form of sodium warfarin in tablets does not present a serious risk in terms of treatment safety [2]. From a safety point of view, the transition of solid sodium warfarin to the poorly soluble, non-ionized acidic form WA can be intensely problematic.

This study aimed to evaluate the potential influence of interactions between the active pharmaceutical ingredient (API) and commonly used excipients on the safety of generic replacement of warfarin sodium tablets. Changes in the solid phase of warfarin were monitored during the accelerated stability study using solid-state NMR spectroscopy and dissolution tests. Tablets containing crystalline or amorphous sodium warfarin were prepared for the study, and commercial warfarin tablets were also used for comparative analysis. During the stability study, the conversion of the warfarin sodium salt to its acidic form through interaction with certain excipients was demonstrated. This solid-phase transformation of warfarin leads to significant changes in the dissolution profile, especially at different API particle sizes in the tablet. Therefore, the choice of appropriate excipients and API particle size are critical factors influencing the safety of generic warfarin sodium.

This study was supported in part by the Ministry of Education, Youth and Sports of the Czech Republic (project LTAUSA18011)

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P24

SYNTHESIS OF HYBRID COMPOUNDS CONTAINING A BENZO[*B*]FURAN AND *N*-ARYLPIPERAZINE SCAFFOLD

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KEYWORDS: BENZO[*B*]FURANS; *N*-ARYLPIPERAZINES; SYNTHESIS; HYBRID COMPOUNDS

The molecular hybridization of privileged structures reflects a conceptual strategy in the design and development of new pharmacologically effective and safe compounds [1]. The increase in incidence of various multidrug-resistant pathogens observed currently is regarded as a very significant public health issue. An effective strategy to counteract antimicrobial resistance is the design and optimisation of hybrid molecules consisting of two or more distinct structural (privileged) motifs [2]. Therefore, the present research aimed at the synthesis of such hybrid compounds containing a benzo[*b*]furan as well as *N*-arylpiperazine fragment. These privileged scaffolds have been recognized as notable building blocks in the structure of promising drug candidates or clinically approved drugs with diverse beneficial biological properties, which include antibacterial, antimycobacterial, and antiviral activity [3, 4]. The objectives of current research were to *a)* optimise a multi-step synthetic process of proposed series of benzo[*b*]furan-2-yl-(4-substituted piperazine-1-yl)methanones, *b)* spectrally verify their identity (^{1}H-NMR, ^{13}C-NMR, and IR), *c)* verify their purity (RP-HPLC), *d)* determine several fundamental physicochemical properties, including solubility and lipophilicity, which can notably affect their pharmacodynamic and pharmacokinetic profile.

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

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P25

THE DESIGN, SYNTHESIS, AND BIOLOGICAL EVALUATION OF BORONIC DERIVATIVES INSPIRED BY THE NONSTEROIDAL ANTI-ANDROGEN ENZALUTAMIDE

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KEYWORDS: NONSTEROIDAL ANTI-ANDROGEN; ENZALUTAMIDE; CASTRATION-RESISTANT PROSTATE CANCER; BORONIC ACID

Due to the development of castration-resistant prostate cancer, that does not respond to second-generation nonsteroidal anti-androgen treatment, significant efforts are being made to develop agents that will antagonise mutant androgen receptor variants and inhibit the binding of testosterone and dihydrotestosterone [1]. According to a recent publication by our team, it is possible to replace the nitro group in the structure of flutamide with a boronic acid functional group [2]. In the structure of later approved non-steroidal antiandrogens, the nitrile functional group is in the same position as the nitro group. We have replaced the nitrile group in enzalutamide structure analogues with a boronic acid residue that includes two oxygen atoms, like the nitro group in the flutamide molecule. Boron can form a dative bond with biological nucleophiles in amino-acid residues. This could lead to the discovery of an agent effective for the treatment of castration-resistant prostate cancer. To investigate the effect of structural modifications on the antiandrogenic activity, hydrophilic, lipophilic, electron-withdrawing and electron-donating groups have been introduced into the structure. Also effect of halogen moiety adjacent to boronic acid group will be studied. Our five-step synthesis process appears to be effective and has been successfully optimised. In the near future, an *in vitro* screening of a preliminary series will be performed using the LAPC-4 androgen-dependent human prostate cell line and the PC-3 androgen-independent human prostate adenocarcinoma cell line. The selectivity of the compounds will also be assessed.

The study was supported by SVV 260 666 (Charles University, Czech Republic).

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P26

FROM FLUSH TO FRESH? - REDUCING PHARMACEUTICALS BY CAVIPLASMA

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KEYWORDS: PHARMACEUTICALS; WATER POLLUTION; PLASMA DISCHARGE; HYDRODYMANIC CAVITATION; LC-MS/MS

Pharmaceutical contaminants from human and veterinary applications, along with improper disposal practices, have become pervasive pollutants in aquatic ecosystems. These substances often evade conventional wastewater treatment systems, resulting in ecological disruption and potential risks to human health [1]. Non-thermal plasma (NTP) has emerged as a promising advanced oxidation process, integrating mechanisms such as ozonation, UV photolysis, and pyrolysis to degrade resistant contaminants. Recent research highlights that the combination of NTP with hydrodynamic cavitation (CaviPlasma) significantly enhances degradation efficiency by improving mass transfer and generating additional reactive species [2].

We applied this technique to degrade selected pharmaceutical compounds that are known to persist in aquatic environments and resist conventional wastewater treatment. After just 12 seconds of treatment, representing a single pass through the device, a minimum degradation of 20% was observed for each of the compounds tested. This initial reduction demonstrates the immediate effectiveness of the CaviPlasma device, even under relatively short exposure times.

Although degradation efficiency varied among the compounds, likely due to differences in molecular structures and reactivity with the generated reactive species, the results confirm the potential of CaviPlasma as a rapid and effective treatment method for a range of pharmaceutical pollutants.

This work was supported by the Technology Agency of the Czech Republic and the Czech Ministry of the Environment under the Environment for Life Programme (project No. SS07020057).

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P27

STABILITY EVALUATION OF HYDROGEL PARTICLES CONTAINING VOLATILE PHYTOTHERAPEUTICS

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KEYWORDS: HYDROGEL PARTICLES; PHYTOTHERAPEUTICS; IONIC GELATION; STABILITY

In recent years, there has been a significant rise in the use of phytotherapy as an alternative strategy for managing a variety of health conditions [1]. Among natural compounds, terpenes and phenylpropanoids stand out due to their broad spectrum of biological activities, including antiviral, antibacterial, antitumor and antioxidant effects. However, their clinical application is often limited by their high volatility and short action duration [2]. Encapsulation of volatile phenolic actives within hydrogel-particle matrices followed by their incorporation into hard capsules represents a promising strategy to enhance drug bioavailability [3]. Due to the limited available data on the long-term stability of this final dosage form, comprehensive stability monitoring is necessary to detect potential losses of volatile active ingredients and to identify adverse physicochemical interactions within the final system.

The aim of this study was to encapsulate natural substances (thymol, eugenol, carvacrol) into hydrogel particles using the external ionic gelation method. The resulting particles were analyzed for their size, sphericity, encapsulation efficiency and antimicrobial activity. They were subsequently filled into hard gelatin capsules and stored under two different storage conditions: in a stability chamber (25 °C, 60 % humidity) and refrigerator (approximately 9 °C, 35 % humidity). Dissolution testing, drug content analysis were performed at the time of preparation and after three months of storage. In addition, the structural and physical properties of the particles were evaluated and compared using scanning electron microscopy (SEM).

The study was supported by MUNI/A/1521/2024.

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P28

PREPARATION OF AMINO-FUNCTIONALIZED THC DERIVATIVES AS POTENTIAL BIOACTIVE COMPOUNDS

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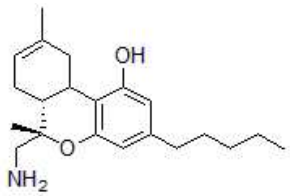
KEYWORDS: TETRAHYDOCANNABINOL; ENDOCANNABINOID SYSTEM

Tetrahydrocannabinol (THC) is the main psychoactive component of *Cannabis sativa* and a ligand of the cannabinoid receptors CB1 and CB2. These G-protein-coupled receptors are part of the endocannabinoid system, which regulates a wide array of physiological processes [1]. Although THC and its analogues exhibits a wide range of biological activities through its interaction with cannabinoid receptors, their clinical use is limited by poor water solubility, psychoactive side effects, and insufficient receptor selectivity [2]. Chemical modification of the THC structure represents a promising strategy to overcome these limitations and generate new compounds with improved pharmacokinetic and pharmacodynamic profiles. The introduction of amino group offers multiple advantages: increased solubility, the ability for salt formation, better receptor interaction via hydrogen bonding or electrostatic forces, and access to a broad range of further derivatization [2].



12-amino-Δ^8-tetrahydrocannabinol

Our approach focuses on modifying a key position on the THC molecule by introducing a hydroxyl group into the structure and then replacing it with an aliphatic amino group. The synthesized compounds were characterized using NMR, mass spectrometry and underwent preliminary biological testing.

The study was supported by MUNI/C/1738/2023.

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P29

STEREOSELECTIVE MICHAEL ADDITION OF BENZO[*b*]THIOPHENE-1,1-DIOXIDE DERIVATIVES

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KEYWORDS: MICHAEL ADDITION; ASYMMETRIC ORGANOCATALYSIS; BENZOTHIOPHENE; ENANTIOSELECTIVITY; DIASTEREOSELECTIVITY

Michael addition is a key carbon–carbon bond-forming reaction between nucleophiles and electron-deficient alkenes. This reaction is highly attractive for stereoselective organocatalysis due to the diverse range of possible nucleophilic and electrophilic partners. Moreover, it enables the synthesis of highly complex molecules in a single step.

Benzo[*b*]thiophene-1,1-dioxide and its derivatives represent a novel class of powerful Michael acceptors. Its structural motif is found in numerous biologically and pharmaceutically active compounds. Additionally, incorporating electron-withdrawing groups into the structure could enhance its reactivity further.

Phenols were found to be the most suitable nucleophilic partners in reactions with benzo[*b*]thiophene-1,1-dioxide derivatives. Benzo[*b*]thiophene-1,1-dioxide substrates were modified and screened to identify the most suitable electrophilic structures. Among the tested compounds, the 2-trifluoromethyl acetyl derivative of benzo[*b*]thiophene-1,1-dioxide displayed the highest reactivity and stereoselectivity. In the next phase, selected chiral bifunctional organocatalysts were examined for their ability to catalyze the stereoselective Michael addition. The resulting products were analyzed using chiral HPLC and NMR techniques to determine enantiomeric ratios (e.r.), diastereomeric ratios (d.r.), and conversion rates. Preliminary experiments yielded Michael adducts with excellent yields and good diastereoselectivity (d.r. up to 86:14), although moderate enantioselectivity was observed (e.r. up to 67:33).

While there is enough room for further improvements, these results highlight the synthetic capability of the benzo[*b*]thiophene-1,1-dioxide scaffold as an appealing electrophilic partner.

The study was supported by Grant Agency of Masaryk University within the Student Research support programme – Excellent diploma thesis, project number MUNI/C/1992/2024.

DEVELOPMENT OF PROLYL-tRNA SYNTHETASE INHIBITORS WITH ANTIPROLIFERATIVE ACTIVITY

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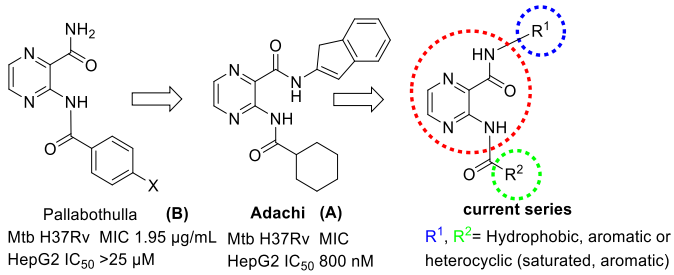
KEYWORDS: ANTICANCER; ANTIMICROBIAL STUDIES; ANTIPROLIFERATIVE; CADD; PROLYL-tRNA SYNTHETASE INHIBITORS; PYRAZINAMIDE

Prolyl-tRNA synthetase (ProRS) is one of the enzymes of the aminoacyl-tRNA synthetase family. **Human ProRS (hsProRS)** is found as a C-terminal domain of combined glutamyl-prolyl-tRNA synthetase. Inhibition of hsProRS has been recognized as a promising approach to treating autoimmune diseases, cancers, and fibrosis [1]. Our goal is to develop potential inhibitors of hsProRS. Our structure scaffold revolves around **3-aminopyrazine-2-carboxamide,** derived from a previously reported hsProRS inhibitor - the Adachi ligand (**A**) [2]. The scaffold with proper modifications has affinity and selectivity to human hsProRS, while some of the synthetic intermediates (without R^1 substituent) are expected to also have antimicrobial activity due to similarity with structures (**B**) published by our group [3]. The published Adachi ligand and its confirmed interactions act as our pharmacophore. The prioritization of substituents was based on molecular docking to hsProRS. The intermediates and the final compounds were sent to biological testing which comprises of complementary antibacterial screening (mycobacteria, clinically relevant G+ and G- bacteria, fungi), cytotoxicity testing on normal human cell lines, and human prostatic cancer cells for antiproliferative activity. We will discuss the *in silico* modelling results and SAR of the prepared compounds.



The study was supported by „The project National Institute of virology and bacteriology (Programme EXCELES, ID Project No. LX22NPO5103) - Funded by the European Union - Next Generation EU. "Additional support was provided by Charles University (SVV 260 666).

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P31

DESIGN AND THERAPEUTIC POTENTIAL OF SEMISYNTHETIC GALANTHAMINE DERIVATIVES

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KEYWORDS: TUBERCULOSIS; AMARYLLIDACEAE; GALANTHAMINE; ANALOUGES; ANTIMYCOBACTERIAL ACTIVITY

Tuberculosis remains a pervasive global health challenge, driven by increasing drug resistance and the limited availability of compounds with novel mechanisms of action. Drug development is hindered by the unique biological barriers of *Mycobacterium tuberculosis*, including its highly lipophilic cell envelope, intracellular persistence within macrophages, and the demand for selective, pharmacokinetically favorable scaffolds [1]. Galanthamine, a tetracyclic Amaryllidaceae alkaloid, was explored as a lead for semisynthetic optimization. Esterification at the 6-hydroxyl position with aromatic acyl chlorides afforded a series of 6-*O*-acyl galanthamine derivatives. Among these, 6-*O*-(4-butylbenzoyl) galanthamine and 6-*O*-(2-naphthoyl) galanthamine exhibited potent antimycobacterial activity with MICs of 3.5 µM and 4.1 µM**,** respectively. Cytotoxicity against HepG2 cells (IC_{50}: 14.7 µM, 21.2 µM) resulted in favorable selectivity indices [2]. Structure–activity relationship analysis indicated that increased lipophilicity at the 6-OH position enhances antimycobacterial potency. Based on these findings, further structural refinement will focus on 6-O-carbamate analogues, ethers, carbamoyl chloride aiming to improve metabolic stability, selectivity, and intracellular efficacy. These results position galanthamine as a promising scaffold for rational anti-TB drug development [3].

The study was supported by from EU-Project "OncoPharm" No. CZ.02.01.01/00/23_021/0008442 and co-funded by Charles University (no. SVV 260 662).

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P32

HPMA-BASED POLYMER CONJUGATES OF CIPROFLOXACIN TARGETED TO BACTERIAL INFECTIONS VIA DEFEROXAMINE (FE^{3+})

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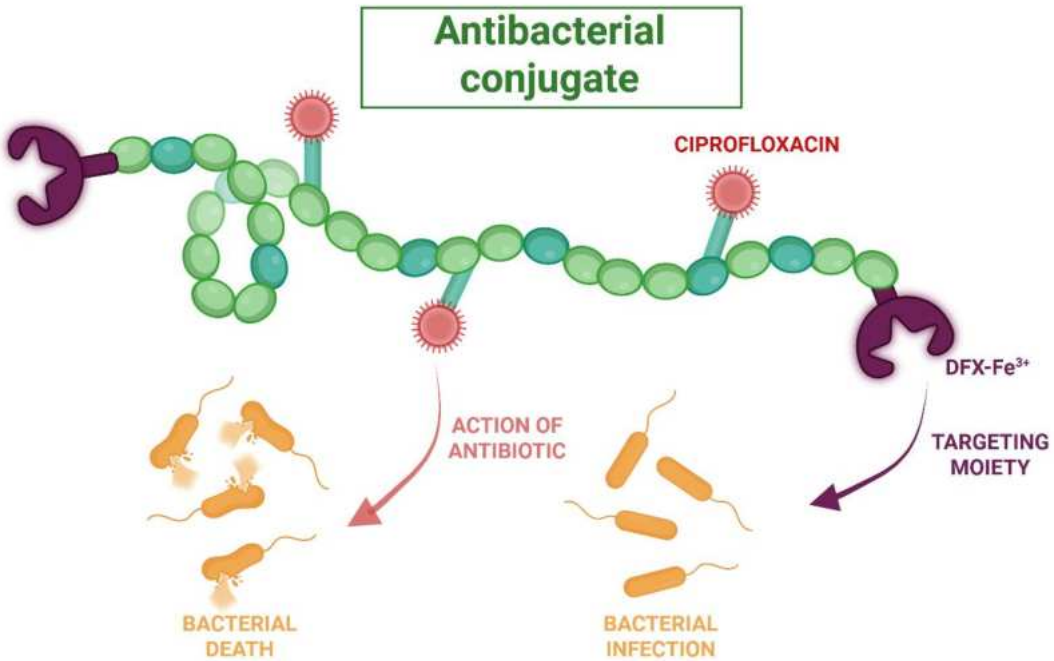
KEYWORDS: POLYMERIC DRUG DELIVERY; TARGETED ANTIBIOTIC THERAPY; HPMA COPOLYMER; CIPROFLOXACIN; ENHANCED BACTERIAL UPTAKE

Polymeric drug delivery systems offer a promising approach for targeted antibiotic therapy, particularly due to their ability to improve the pharmacokinetic properties of active compounds, reduce systemic toxicity, and enable selective accumulation at sites of infection. In this work, we present a novel polymer conjugate based on a hydrophilic N-(2-Hydroxypropyl) methacrylamide (HPMA) copolymer carrier, incorporating two key components: the antibiotic ciprofloxacin and a complex of deferoxamine with iron (DFX-Fe^{3+}). Ciprofloxacin provides antimicrobial activity, while the DFX-Fe^{3+} complex serves as a targeting moiety, exploiting the iron-scavenging behavior of bacteria that actively uptake iron from their surroundings to support growth. This strategy enables preferential accumulation of the conjugate at the site of bacterial infection. In vitro studies confirm that the antibacterial activity of ciprofloxacin is retained and demonstrate enhanced uptake of the conjugate by bacterial cells compared to the free antibiotic. The presented system shows strong potential for the development of more effective and selectively acting antimicrobial.



ELEMENTAL ANALYSIS OF HONEY SAMPLES

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KEYWORDS: X-RAY FLUORESCENCE ANALYSIS; HONEY; INORGANIC ELEMENTS; HEAVY METALS

Honey, as a food product, is regulated by the internationally recognised Codex Alimentarius – Standard for Honey. It should not contain heavy metals in concentrations that can impair human health upon consumption. The limits are established by the Codex Alimentarius Commission [1]. A maximum concentration of 0.1 mg/kg for lead in honey is set, while currently no limits are specified for other heavy metals [2]. The subject of our work was the identification and quantification of chemical elements in different honeys (80 samples) by energy-dispersive X-ray fluorescence analysis, including goldenrod, acacia, rapeseed, sunflower, linden, milkweed, horse chestnut, hawthorn, common sea-lavender, fennel, buckwheat, raspberry, pine, thyme, honeydew, and mixed blossom honey, collected from different geographical locations. Honeys were collected between 2020 and 2025. We identified and quantified these elements in the respective samples: ^{11}Na, ^{13}Al, ^{15}P, ^{19}K, ^{20}Ca, ^{26}Fe, ^{27}Co, and ^{30}Zn. The presence of these elements showed considerable variations. Other identified elements (^{21}Sc, ^{25}Mn, ^{29}Cu, ^{31}Ga, ^{34}Se, ^{35}Br, ^{46}Pd, ^{48}Cd, ^{49}In, ^{52}Te, ^{53}I, ^{54}Xe, ^{56}Ba, ^{58}Ce, ^{63}Eu, ^{64}Gd, ^{65}Tb, ^{66}Dy, ^{67}Ho, ^{68}Er, ^{69}Tm, ^{77}Ir) could not be quantified due to the lack of available salts suitable for calibration. Honey is an excellent source of ^{20}Ca. The specific values of the quantified elements will be presented in the poster and later in the publication. The amounts of the monitored heavy metals in our samples were below the limits specified in Ph. Eur. 11 and the Codex Alimentarius Commission, which means that our plant materials can be considered to be from an ecologically clean locality.

The study was supported by grant projects FaF/10/2025, VEGA 1/0226/22, VEGA 1/0101/23, CEEPUS M-RS-1113-2425-192286 and CEEPUS RS-1113-08-2425.

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ISATIN DERIVATIVES-POTENTIAL DRUGS

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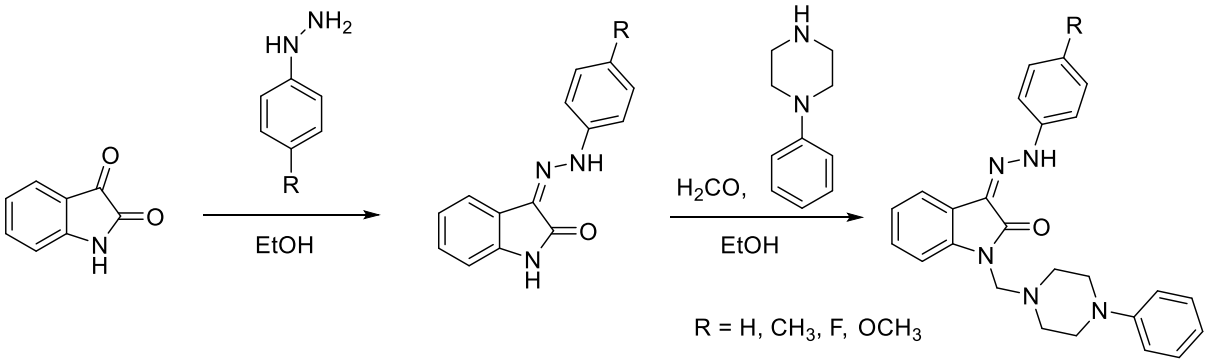

The research is focused on the synthesis, characterization and study of the biological properties of isatin derivatives as suitable candidates for new drugs. Isatin and its derivatives belong to the organic compounds used in chemical practice. They are used primarily in areas such as medicinal chemistry (e.g. as antibiotics, antimalarials, etc.), in the field of nanotechnology, development of analytical reagents and dyes, and in the field of synthesis of heterocyclic compounds and stereoselective procedures. Isatin undergoes various modifications easily, therefore its derivatives belong to the class of privileged heterocyclic structures [1], on the basis of which biologically active substances of a wide spectrum of action have been proposed. Therefore, the majority of publications about the synthesis and reactions of isatin and its derivatives belong to the field of pharmaceutical chemistry [2]. The aim of the work was the synthesis of new, not yet described in the literature, derivatives of 3-(phenylhydrazono)isatin with a phenylpiperazine substituent in the N-1 position [3].

The study was supported by APVV-22-0133.

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ANILINE DERIVATIVES AS POTENT CARBONIC ANHYDRASE INHIBITORS

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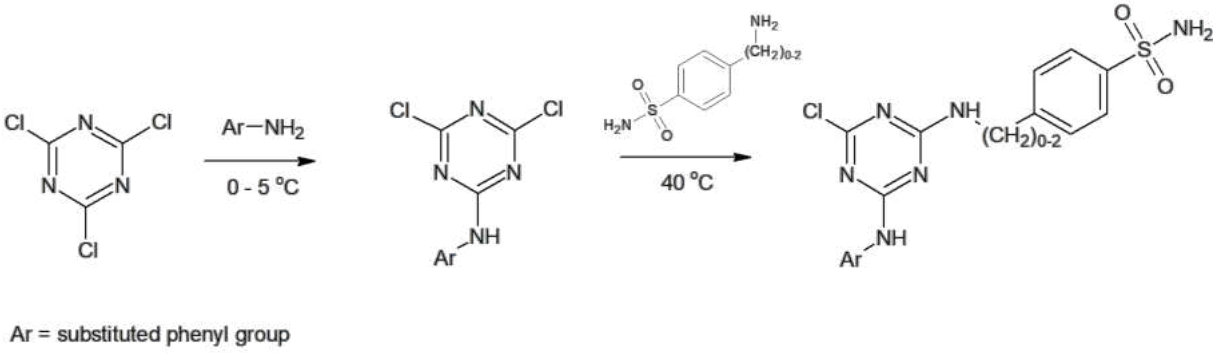
KEYWORDS: CARBONIC ANHYDRASE INHIBITION; TRIAZINE; BENZENESULFONAMIDE; ANILINE



General scheme for synthesis of target 1,3,5-triazine derivatives.

Carbonic anhydrases are omnipresent metalloenzymes that catalyze reversible conversion of carbon dioxide to bicarbonate and proton, maintaining homeostasis. In humans, they are involved in multiple physiological processes, and they are linked to many disorders, such as glaucoma, neurodegeneration or cancer. Their potential inhibition is of considerable interest in biomedical research. [1]. In bacteria, inhibition of carbonic anhydrases leads to inhibition of their growth and makes them more vulnerable to host defense mechanisms [2].

Based on our previous findings, where a lead 1,3,5-triazinyl aminobenzenesulfonamide incorporating an aniline motif exhibited high inhibitory activity against carbonic anhydrase (K_i = 7.4 nM against CA IX), a new serie of related derivatives was designed and synthetised to further explore structure–activity relationshis and to improve their selectivity. The new compounds were evaluated for their inhibitory activity against various CA isoforms.

The study was supported by project MUNI/A/1474/2024 and Interdisciplinary project MUNI/G/1002/2021.

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POLYSACCHARIDE-BASED COLUMNS AS A TOOL FOR CHIRAL SEPARATIONS OF CARBORANES

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KEYWORDS: CHROMATOGRAPHY; BORONE CLUSTER COMPOUNDS; POLYSACCHARIDE COLUMNS

Cobalt bis(dicarbollide) and *nido*-7,8-dicarbaundecaborate derivatives are notable for their high stability and hydrophobic nature, sparking interest in pharmaceutical research due to their function as 3D platforms for pharmacophores [1]. Some of these compounds can exhibit “at cage“ chirality, primarily due to asymmetric substitution. Chirality is a significant feature in pharmaceutical chemistry, because of possible difference in pharmacokinetics of enantiomers. The development of efficient and reliable methods for enantiomeric separation is then crucial for advancing research and potential applications of carborane-based drugs [2]. This study is focused on primary research dealing with chiral separations of chiral cobalt bis(dicarbollides) and *nido*-7,8-dicarbaundecaborates in HPLC using polysaccharide-based columns. Initial chiral screening was performed under gradient conditions, building on an isocratic method previously established by our research group [2]. The scope of chiral selectors and analytes was broadened in this work. The chiral method was optimized for each analyte in isocratic elution, achieving baseline separation for 73 % of racemic mixtures. Zwitterionic compounds showed better separation on amylose-based columns compared to anions. Conversely, cobalt bis(dicarbollide) anions were more effectively separated on cellulose-based columns. *Nido*-7,8-dicarbaundecaborate anion derivatives are challenging for chiral separations, with only a few racemic mixtures resolved into enantiomers up to date. [3,4]. In this study, we successfully achieved baseline separation of [7-C_6H_5-7,8-nido-$C_2B_9H_{11}$] [$(CH_3)_4N$] on polysaccharide-based columns for the first time.

The study was supported by The Czech Science Foundation (project n. 25-16216S) and Charles University Grant Agency (GAUK n. 368425).

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SYNTHESIS OF CHIRAL EXOCYCLIC AMIDINES VIA TANDEM REDUCTION/CYCLIZATION CASCADE USING SODIUM BIS(2-METHOXYETHOXY)ALUMINIUM HYDRIDE

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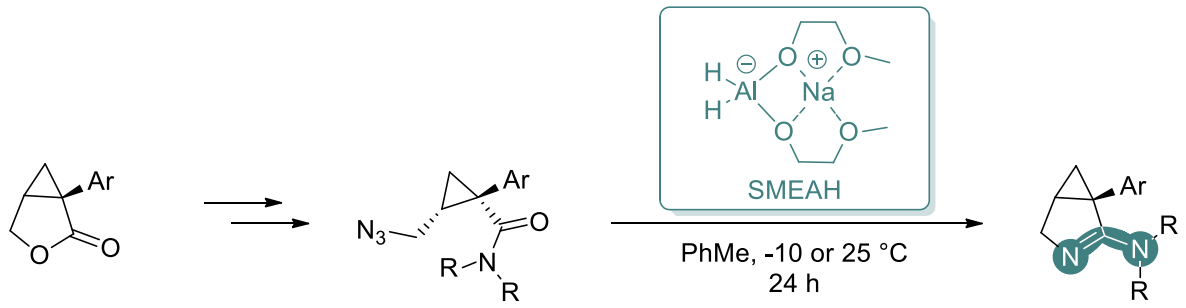
KEYWORDS: AMIDINE; ORGANOCATALYST; SUPERBASE

Chiral amidines have emerged as a valuable class of organocatalysts due to their strong Brønsted basicity, structural tunability, and capacity for stereoselective induction. Their ability to activate electrophiles through hydrogen bonding or ion pairing makes them particularly effective in a variety of asymmetric reactions [1]. Sodium bis(2-methoxyethoxy)aluminium hydride (SMEAH, Synhydrid®, Red-Al®) as a reducing agent evinces remarkable reactivity in certain cases compared to other commonly used reagents like $LiAlH_4$ or diisobutylaluminum hydride (DIBAL-H) [2]. In our study, we developed a synthetic strategy to generate a novel type of chiral exocyclic amidines featuring an azabicyclo[3.1.0]hexane core. The key reaction step involves tandem reduction/cyclization of azido-amide derivatives promoted by SMEAH, which takes advantage of the ipsilateral effect of *cis*-1,2-cyclopropane substituents. Using optimized reaction conditions, we successfully obtained a series of target molecules with different Ar and *N*-substituents in good yields. The products thereof represent structurally unique, tunable, superbases with promising applications in enantioselective catalysis.



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SYNTHESIS AND PHARMACOLOGICAL TESTING OF NEW ARYLOXYAMINOPROPANOL DERIVATIVES

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KEYWORDS: SYNTHESIS; ARYLOXYAMINOPROPANOL; VIABILITY; HUMAN EMBRYONIC KIDNEY CELLS

Aryloxyaminopropanol drugs are a class of pharmaceuticals, often recognized for their beta-blocking properties that are used in the treatment of various cardiovascular conditions like: treatment of tachycardia, hypertension, myocardial infarction, congestive heart failure, cardiac arrhythmias, coronary artery disease, hyperthyroidism, essential tremor, aortic dissection, portal hypertension, glaucoma [1, 2]. The thesis deals with the synthesis of new derivatives containing an aryloxyaminopropanol pharmacophore in their molecule, which makes these derivatives attractive in terms of potential use as drugs, beta-blockers. Four selected derivatives **1,2a-b** were tested for their cytotoxicity on human embryonic kidney cells at concentrations ranging from 6.25 µM to 100 µM.

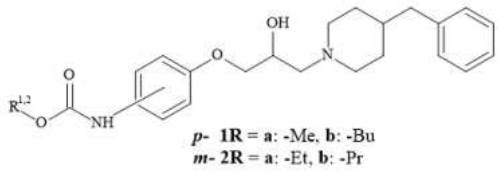

Fig. 1: Chemical structure of tested derivatives **1,2a-b**

Assessment of cellular response to test substance exposure was conducted every hour during 48 hours using the xCELLigence system that monitors cell behaviour (adherence, proliferation, morphology). The change in cell adherence was dependent on the concentration of derivatives **1,2a-b** (the higher the concentration, the greater the change in cellular response).

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LASER-ABLATION SPECTROSCOPY TECHNIQUES IN CANCER BIOMARKER DETECTION AND IMAGING

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KEYWORDS: LIBS; LA-ICP-MS; CANCER BIOMARKERS; IMMUNOCYTOCHEMISTRY; NANOPARTICLES

Immunochemical methods offer rapid detection of biomarkers associated with specific diseases by appropriately labeled antibodies [1]. Laser ablation spectroscopy is emerging as a promising tool in molecular oncology due to its ability to combine elemental detection with spatially resolved imaging [2]. This study evaluates the performance of three elemental tags, Lu-MAXPAR, gold nanoparticles (AuNPs), and upconversion nanoparticles (UCNPs), for the detection of the HER2 protein using immunocytochemistry measured by Laser-Induced Breakdown Spectroscopy (LIBS). BT-474 breast cancer cells, preserved as formalin-fixed paraffin-embedded pellets, served as HER2-positive models, while MDA-MB-231 cells were used as negative controls. Based on the experimental results, UCNPs appear to be the most suitable labels in combination with LIBS. The integration of LIBS and UCNPs thus offers a rapid and multiplexable strategy for cancer biomarker detection in clinically relevant samples. Additionally, in this study, the performance of LIBS-based detection is compared to Laser Ablation Inductively Coupled Plasma Mass Spectrometry (LA-ICP-MS), a pioneer laser ablation technique for peptide/protein marker analysis via elemental labeling and simultaneous mapping of the natural distribution of elements [3].

The study was supported by the Czech Science Foundation (GACR: GA25-16166S) and Masaryk University Foundation (MUNI/A/1790/2024).

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mTOR INVOLVEMENT IN INFLAMMATION-INDUCED CHANGES OF LIPID METABOLISM IN HEPG2 CELLS AND ACTIVITY OF mTOR INHIBITOR EVEROLIMUS

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KEYWORDS: mTOR, INFLAMMATION, EVEROLIMUS

Inflammation and lipid metabolism are tightly interconnected. Chronic inflammatory diseases are associated with alterations in lipid metabolism, increasing the risk of atherosclerosis [1]. Several studies highlight deregulation of the mTOR pathway as a typical feature of inflammatory conditions in the liver. In this study, we aimed to investigate the involvement of mTOR in the inflammatory remodeling of lipid metabolism in vitro, and in particular, to examine the effect and activity of the mTOR inhibitor everolimus. An inflammatory environment in HepG2 cells was induced by CM from THP-1 stimulated with PMA and LPS. The role of the mTOR pathway was assesed using its inhibitor, rapalog everolimus. The changes in mRNA expression of target genes were tested by RT-PCR and protein expression by western blot. CM stimulation led to increased expression of LDLr and decreased expression of PCSK9 in HepG2 cells. According to the literature, such changes are indicative of enhanced mTOR pathway activity. This assumption is further supported by our preliminary western blot results, which showed increased mTOR phosphorylation, suggesting activation of the pathway. Surprisingly, attempt to inhibit the mTOR activity with everolimus leads to exacerbated effect on PCSK9 (further decrease) and LDLr (further increase) expression. These findings may reflect the complexity of mTOR signaling in lipid regulation, or indicate that everolimus may exert specific effects beyond classical mTOR inhibition. Understanding these mechanisms could provide valuable insights into inflammation-driven changes in lipid metabolism and the therapeutic potential or limitations of rapalogs like everolimus.

Funded by the EU NextGenerationEU through the Recovery and Resilience Plan for Slovakia under the project No. 09I03-03-V05-00012.

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Industrial Talk

IT01

UTILISATION OF RAMAN OPTICAL ACTIVITY IN DRUG ANALYSIS

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KEYWORDS: RAMAN OPTICAL ACTIVITY; ENANTIOMERIC EXCESS; CHIRAL DRUGS

Raman optical activity (ROA) involves measuring the small difference in the Raman scattering of chiral molecules in relation to right- and left-circularly polarised radiation. ROA was discovered more than 50 years ago and has since undergone intensive development, resulting in a wide range of applications. ROA has been used to study various organic molecules, natural products [1-2], medicines and drugs [3-4], and can be applied to the structural analysis of proteins, nucleic acids and viruses [5]. ROA can also be used for disease diagnosis through the spectral analysis of body fluids [6].

As well as providing information on structure, dynamic behavior and intermolecular interactions [7], ROA is primarily used to determine the absolute configuration of molecules and identify diastereoisomers [8]. One of the most promising applications of ROA is determining enantiomeric excess (ee). We have demonstrated that ROA can achieve an accuracy of ee determination less than 0.05% [9], which is difficult to attain using other analytical techniques.

At the Department of Optics, in cooperation with ZEBR company, we are developing ROA spectrometers for use in medical and industrial applications. The spectrometers are characterized by quality of spectra, high signal to noise ratio, robustness and stability, which are crucial for use in the pharmaceutical industry.

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Sponsor Talks

(U)HPLC AGILENT INFINITY III – KEY TO HIGHER PRODUCTIVITY AND QUALITY IN PHARMACEUTICAL LABORATORIES

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The latest generation of Agilent Infinity III liquid chromatographs represents a significant step forward, combining proven reliability with innovative features specifically designed to meet the stringent requirements of pharmaceutical laboratories and GxP regulated environments. The goal is to maximize the efficiency and reliability of analytical processes, from research and development of new drugs to routine quality control (QC) of final products. The system's intelligent features fundamentally simplify work, minimize the risk of human error, and ensure continuous operation, which is crucial in pharmaceuticals.

For example, InfinityLab Level Sensing, a proactive mobile phase level monitoring system, uses precise gravimetric measurement and consumption prediction to prevent unplanned system shutdowns during analysis. This is invaluable for ensuring data integrity during long sequences typical of pharmaceutical stability studies or large batch sample analyses during batch release, where any interruption means loss of time and resources.

Another pillar, the InfinityLab Assist Interface, functions as an intelligent assistant with a touch interface that enables automation of routine tasks such as system preparation or flushing, which is ideal for optimizing shift work in pharmaceutical QC operations. It also offers remote monitoring and, most importantly, integrated guides for quick diagnostics and troubleshooting or scheduled maintenance, thereby minimizing critical downtime and helping to maintain system compliance with System Suitability Test (SST) requirements.

For pharmaceutical laboratories processing hundreds of samples daily, the InfinityLab Sample ID Reader is crucial. The integrated QR code reader automatically identifies each sample and links it to the results, eliminating the risk of mix-ups – a common cause of costly OOS (Out-of-Specification) investigations in pharmaceuticals – and ensuring flawless traceability and data integrity for audit and regulatory compliance purposes.

In addition to these smart features, Infinity III offers state-of-the-art chromatographic parameters, including bio-inert variants for biopharmaceutical analysis, and maintains full backward compatibility, allowing pharmaceutical companies to easily transfer and utilize already validated analytical methods without the need for costly revalidation.

Agilent Infinity III thus represents a robust and intelligent solution that enhances productivity, reliability, and regulatory compliance of pharmaceutical laboratories.

ANTON PAAR – SOLUTION FOR THE PHARMACEUTICAL INDUSTRY

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KEYWORDS: PRODUCT PORTFOLIO; PHARMACEUTICAL POWDERS

Introduction to Anton Paar product portfolio which can solving key challenges with pharmaceutical powders like: maintaining consistent solubility and dissolution rates, monitoring flow properties under real-life environmental conditions, achieving uniform packing and tableting, analyzing formulation stability, detecting and avoiding heavy metal contamination, identifying samples, compliance with 21 CFR Part 11.

LOW-VOLTAGE TRANSMISSION ELECTRON MICROSCOPY (LVEM) FOR HIGH-CONTRAST IMAGING IN PHARMACEUTICAL RESEARCH: FROM VIRUSES TO NANOCARRIERS

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KEYWORDS: LOW-VOLTAGE TRANSMISSION ELECTRON MICROSCOPY (LVEM); MULTIMODAL IMAGING; HIGH-CONTRAST IMAGING; DRUG DELIVERY NANOPARTICLES

Lipid-based nanoparticles are increasingly employed in modern drug delivery systems, gene therapies, and vaccines due to their biocompatibility, encapsulation efficiency, and structural versatility [1]. Comprehensive nanoscale characterization of such systems is crucial for understanding structure–function relationships and ensuring reproducibility in pharmaceutical development. While conventional high-voltage TEM provides the resolution required, its application to light-element samples such as lipids and proteins is often limited by poor image contrast and demanding infrastructure requirements [2].

Low-Voltage Transmission Electron Microscopy (LVEM) addresses these challenges by operating at accelerating voltages between 5 and 25 kV, thereby enhancing contrast for light-element materials and allowing detailed visualization of nanoparticles and biomolecules with minimal or no staining [2]. This reduces preparation artifacts and simplifies workflows. In this presentation, we will introduce the LVEM family of instruments developed by Delong Instruments, including the LVEM 25E and LVEM 5, both compact systems optimized for biological and pharmaceutical applications. The LVEM 25E is a compact all-in-one system integrating multimodal imaging capabilities—TEM, STEM, SEM (BSE), dark-field TEM/STEM, EDS, and electron diffraction—at resolutions down to 1 nm. The LVEM 5, a benchtop TEM operating at 5 kV with 1.2 nm resolution, provides exceptional contrast for particle-like samples. Case studies will illustrate applications of LVEMs in imaging lipid-based nanocarriers, viral vectors, polymeric nanoparticles, and graphene-based materials [3]. By combining high-contrast performance, multimodal versatility, compact design, and minimal infrastructure requirements, LVEMs offer a powerful and accessible solution for pharmaceutical research and industry including quality control.

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WELCOME TO THE FAMILY BUSSINES OF TH. GEYER – WITH THE HELP OF SIOT

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KEYWORDS: SIOT; TH. GEYER; LABSOLUTE; CHEMSOLUTE; BIOSOLUTE

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FROM DATA TO DISCOVERY:
LEVERAGING DIGITAL SOLUTIONS IN CHEMICAL SYNTHESIS AND ANALYSIS

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KEYWORDS: DIGITAL CHEMISTRY; AI SOLUTIONS; DRUG DISCOVERY

In the evolving landscape of chemical research, digital solutions are transforming synthesis and analytics. This company talk will explore how Merck leverages innovative digital technologies to enhance productivity and drive scientific breakthroughs across all stages of drug discovery workflow.

We will introduce AIDDISON, our AI-powered drug discovery platform that utilizes over 30 years of pharmaceutical data to streamline the discovery process. AIDDISON enables rapid *in silico* screening, helping researchers optimize results for synthesizability and ADMET properties. Next, we'll briefly touch SYNTHIA, our unique retrosynthesis software that simplifies the discovery of novel pathways for target molecules. SYNTHIA allows scientists to quickly scan hundreds of pathways, facilitating efficient, cost-effective and if desired also greener route design. CATALEXIS will be highlighted as a catalyst screening platform that optimizes palladium-catalyzed reactions using AI-powered ligand selection, enhancing decision-making and reducing material waste. Additionally, ALDRICH MARKET SELECT service simplifies procurement by providing access to over 14 million on stock chemicals and building blocks, streamlining the transition from virtual design to fast practical bench execution.

We will also showcase MQUANT STRIPSCAN, a mobile phone app that provides fast and reliable pH and concentration determinations using classical MQuant test strips. The session will also cover basics of TLC EXPLORER, a user-friendly platform for thin-layer chromatography that enhances data visualization and interpretation, making analytical processes more accessible. Finally, we will present CHEMISTWIN, a digital reference material tool that automates NMR and IR analysis, ensuring reliable results and enhancing the quality and safety of medicines throughout research and development.

Join this company presentation to discover how these data driven digital solutions from Merck are reshaping chemistry and empowering researchers to achieve greater efficiency and creativity.

References:

www.sigmaaldrich.com

www.digitalchemistry.ai

NANOPHOTONIC EVANESCENCE FIELD SENSING – FUTURE OF IMMOBILIZATION TECHNIQUES

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KEYWORDS: NES; IMMOBILIZATION; PROTEIN INTERACTIONS; WAVEGUIDE

Delta Life Science's pioneering Nanophotonic Evanescent Field Sensing (NES) technology is redefining the landscape of biosensing by integrating advanced photonic circuits with high-sensitivity, multiplexed detection capabilities. At the core of the platform is the innovative inQuiQ® instrument, which utilizes silicon chip-based ring resonators to confine light at the nanoscale, generating evanescent fields that enable real-time detection of biomolecular interactions with exceptional precision. This label-free technique operates on principles similar to Surface Plasmon Resonance (SPR), but surpasses traditional approaches through its compactness, scalability, and ability to conduct multiplex analyses—processing multiple targets in parallel without loss of sensitivity.

The NES system's sensitivity is remarkable, capable of resolving minute changes in refractive index with baseline noise as low as 0.01 RU at a 1Hz read-out, thus facilitating detection down to small molecules and subtle conformational changes in proteins. Its compact photonic chip design not only ensures a cost-effective solution but also enables broad accessibility for life science researchers and pharmaceutical developers, accelerating workflows and enhancing productivity compared to bulky, single-analyte biosensors. The versatility of the NES platform extends beyond drug discovery; potential applications range from medical diagnostics to food allergen analysis and environmental nutrient monitoring, empowering researchers to study molecular-level phenomena with unprecedented accuracy.

In summary, Delta Life Science's nanophotonic evanescent field sensing technology offers an affordable, highly accurate, and user-friendly biosensing solution, poised to advance scientific research and healthcare diagnostics by delivering rapid, reliable insights into molecular interactions. [1]

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