Program and Abstracts

5th International Conference on Integrative Chemistry, Biology & Translational Medicine

ICBTM 2026

a hub of knowledge, skills and opportunities

Debrecen, Hungary, 25-27 June 2026

दिल्ली विश्वविद्यालय
University of Delhi

MTA HUNGARIAN ACADEMY OF SCIENCES

Program of the conference

	1st day 25th of June, Thursday			2nd day 26th of June, Friday				3rd day 27th of June, Saturday	
			9:00 - 9:45	Plenary lecture **Roland Pieters**				9:00 - 9:45	Plenary lecture **Peter Preiser**
			9:45 - 10:15	Keynote lecture **Michaela Wimmerova**				9:45 - 10:15	Keynote lecture **Brijesh Rathi**
			10:15 - 10:45	Coffee break				10:15-10:45	Keynote lecture **Pulin K. Gupta**
11:00 - 16:00	**Registration**		Session name		IV. Conference on Therapeutical Purposes (TKP2021-EGA-18 and TKP2021-EGA 19)			10:45 - 11:15	Ravi Durvasula
			10:45 - 11:15	Keynote lecture **Seonghun Kim**	10:45-10:50	Szilvássy Zoltán Ildikó Bácskay Welcome remarks		11:15 – 11:30	Closing ceremony and announcement of poster session winner
					10:50-11:05	Ágnes Rusznyák			
					11:05-11:20	Miklós Vecsernyés			
			11:15-11:45	Keynote lecture **Marko Anderluh**	11:20-11:35	Beatrix Dienes		11:30 -	Excursion to Hortobágy
					11:35-11:50	Rudolf Gesztelyi			
			11:45 - 12:15	Keynote lecture **Vishal Rai**	11:50-12:05	László Kardos			
			12:15 - 12:25	Break					
			12:25 - 13:30	Lunch					
13:00 - 13:15	Opening ceremony		Session name	Young Researchers' Forum	Carbohydrate, Nucleic Acid and Antibiotics Working Committee		IV. Conference on Therapeutical Purposes		
13:15 - 14:00	Plenary lecture **Jayanta Haldar**		13:30-13:45	Keynote lecture **Ronaldo N. de Oliveira**	**Closed meeting**		Dénes Páll		
			13:45-14:00				Béla Juhász		
14:00 - 14:45	Plenary lecture **Caitriona M. O'Driscoll**		14:00 - 14:15	Mansi Verma	Keynote lecture **Barbara Richichi**		Rita Kiss		
			14:15 - 14:30	Ankush Gupta			Zsolt Ráduly		
			14:30 - 14:45	Thi Cam Tu Nguyen	Miklós Lovas		András Szilágyi		
14:45 - 15:15	Coffee break		14:45 - 15:00	Richárd Kajtár	Nawar Ahmad				
Session name		HUPHAR special session	15:00 - 15:20	Coffee break					
15:15 - 15:45	Keynote lecture **Jan Weber**	Keynote lecture **Anil Chuturgoon**							
15:45 - 16:15	Keynote lecture **Lindomar Pena**	Keynote lecture **Jadwiga Handzlik**	15:20 - 15:35	Himanshi Sharma	Rasha Ghanem Kattoub		(Zoltán Szabó) Balázs Palcsik		
			15:35 - 15:50	Padam Raj Bhatt	István Kacsir		Attila Bácsi		
16:15 - 16:30	Martin Zoltner	Krisztina Mária Szabó	15:50 - 16:05	Mohammadamin Biglarikhoshmaram	Ágnes Homolya		Eszter Lilla Tóth		
16:30 - 16:45	Ferenc Dániel Petróczi	Gyula Batta	16:05 - 16:20	Simon Eskeif	Lajos Kovács		Miklós Zrínyi		
			16:20 - 16:35	Zsanett Szilágyi	István Kese				
16:40 - 17:00	Break		16:35 - 16:50	Mária Fanni Boncz	Zsolt Ürögi				
17:00 - 18:00	Poster Session		16:50 - 17:05	Bálint Lakó	Viktória Goldschmidt Gőz				
			17:05 - 17:20	Boglárka Polónyi					
18:00 -	Welcome Reception		17:05 - 19:00						
			19:00 -	Gala dinner					

Abstracts of invited speakers

PL1

Targeting the cell envelope: a versatile antibacterial strategy

Prof. Jayanta Haldar[a]

[a]*Antimicrobial Research Laboratory, New Chemistry Unit and School of Advanced Materials, Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bangalore, India*

E-mail: jayanta@jncasr.ac.in
Web: http://www.jncasr.ac.in/jayanta/

The problem of antimicrobial resistance has escalated rapidly over the years with multidrug-resistant pathogens emerging to existing antibiotic therapy. Conventional antibiotics often target specific metabolic processes in bacteria, thereby often limiting their efficacy against metabolically dormant cells and show high propensity of resistance development.

Antimicrobial peptides produced in the body in response to infection have a non-specific mechanism of action due to their amphipathic structure which results in interaction with the cell envelope in bacteria and other pathogens. However, the success of AMPs is limited by their high in-vivo toxicity, in-vivo degradation and high manufacturing costs. Taking inspiration from AMPs and to solve problems associated with them, my lab has developed amphipathic small molecules containing structural features of peptidomimetics and peptides like amino acids, amide bonds and a hydrophobic group using simple synthetic strategy and optimized their design to attain in-vivo stability and low toxicity. These small molecules have been employed as active membrane-active compounds or weak membrane-perturbing antibiotic adjuvants to revitalize obsolete antibiotics [1-5].

The non-specific mechanism of action results in broad-spectrum activity against drug-resistant bacteria and fungi while also showing potential against adaptive resistance elements like biofilms, persisters and intracellular infection. Further, the antibiotic adjuvants exhibit properties like autophagy induction and antigen-responsive immunomodulation which are instrumental in tackling more complicated forms of infection and inflammation [2-4].

The efficacy of optimized systems has been validated in-vivo and detailed mechanistic insights have been gathered to obtain a holistic understanding. In my talk, I'll be covering all these facets of broad-spectrum amphipathic small molecules, and highlight their immense potential in the fight against antimicrobial resistance. The novel approaches to overcome acquired, intrinsic and adoptive bacterial resistance towards glycopeptides, via semisynthetic modifications of vancomycin will also be discussed [6-8].

[1] G. Dhanda *et al. ACS Cent. Sci.* **2025**, *11*, 279.
[2] R. Dey *et al. Chem. Sci.* **2024**, *15*, 259.
[3] S. Barman *et al. Adv. Therap.* **2022**, *2100234*, 1.
[4] G. Dhanda *et al. ACS Infect. Dis.* **2022**, *8*, 10861097.
[5] R. Dey *et al. Adv. Healthc. Mater.* **2022**, *11*, 2200536.
[6] P. Sarkar *et al. Chem. Sci.* **2023**, *14*, 2386-2398.
[7] Y. Acharya *et al. Chem. Comm.* **2022**, *58*, 1881-1897.
[8] P. Sarkar *et al. ACS Chem. Biol*, **2020**, *15*, 884-889.

PL2

Cyclodextrin nanoparticles: advancing RNA medicines for chronic diseases

Caitriona O'Driscoll[a,b]

Professor of Pharmaceutics

[a]*Coordinator of GENEGUT, Horizon Europe (https://genegut.eu/)*
[b]*Director of Future Medicines, University College Cork, Ireland*

E-mail: caitriona.odriscoll@ucc.ie

The success of the Covid-19 mRNA vaccine illustrated the safey and efficacy of RNA therapeutics for infectious disease. Attention is now focused on the application of RNA to treat non-infectious chronic diseases. Targeting these more complex conditions requires a more innovative delivery approach in order to reach specific disease sites.

Crohn's disease is a chronic disease affecting an increasing number of patients globally. The available therapies are not fit for purpose and often provide only symptomatic relief. The disease has a signifiant negative effect on the quality of life of patients, many utimately require surgery, the loss of time in work and hospitalisation pose a high burden on healthcare costs for patients and healthcare providers. Consequently, an urgent need exists to develop new advanced, effective therapies including those based on RNA.

The 'first generation' of cyclodextrins (CDs) are widely employed as excipients to enhance the solubility of poorly water soluble small molecules via inclusion complex formation. More recently, 'second generation' CDs have been explored as delivery platforms for macromolecules including RNA. By exploiting the geometry of the CD ring structure as a scaffold, functional groups can be conjugated in order to enhance loading, stability, delivery and efficacy of RNA.

The development of an orally administered RNA medicine for the treatment of Crohn's disease is particulary attractive as a patient friendly product which can facilitate local delivery to the inflammed gut wall, thus avoiding potential side effects from systemic exposure. In the GENEGUT project, CD-based nanoparticles incorporationg RNA have been designed, characterised and evaluated for the ability to facilitate oral administration and navigate the barriers to intestinal delivery. A structure activity study has identified lead CD derivatives as potential biomaterials for oral RNA delivery thus paving the way for clinical translation.

Acknowledgement: *GENEGUT (https://genegut.eu/) project funded by the European Commission as a Horizon Europe Research and Innovation Action (RIA) under the call tools and technologies for a healthy society (2021) (HORIZON-HLTH- 2021-TOOL-06, GA 101057491).*

PL3

Inhibiting protein carbohydrate binding by multivalency, virtual screening and DNA-encoded libraries

Roland J. Pieters[a]

[a]*Department of Chemical Biology and Drug Discovery, Utrecht University, 3584 CG, Utrecht, the Netherlands*

E-mail: r.j.pieters@uu.nl

Protein carbohydrate interactions play important roles in biological processes. Similarly, they are involved in processes leading to disease, in areas of infection, cancer and others. Creating therapeutics based on these processes has remained problematic. Carbohydrate-based inhibitors are limited by poor absorption, rapid excretion or degradation and low affinities. Affinities can be enhanced by using multivalency, i.e. linking several carbohydrate ligands together within a single molecule, often matching a protein target with multiple binding sites. Several systems will be discussed based on different binding site orientations. A rigid linkage between ligands was shown to be beneficial for blocking the *P. aeruginosa* LecA with close to three orders of magnitude affinity enhancement. A higher number of binding sites as in the cholera toxin, can best be blocked with a limited number of glycans with spacers of adequate length enabling simultaneous binding, again leading to orders of magnitude enhancements. Polymeric ligands, i.e. higher valency systems, with a less well-defined geometry, may often be a practical solution, for effective binding of readily made systems. Beside this advantage, systems like the Siglecs actually require such systems for optimal activation.

Besides the multivalency approach, we also have used computational virtual screening approaches and DNA-encoded libraires to find non-carbohydrate ligands for carbohydrate binding or processing proteins. Hits were found in all cases, where lectins are the most challenging, while enzymes with a UDP binding site proved to be more amenable to inhibition with non-sugars. Examples and implications are discussed.

PL4

Discovering new target space for the development of drugs against malaria parasites

Peter Preiser[a]

[a]*School of Biological Sciences, Nanyang Technological University, 639798, Singapore*

E-mail: prpreiser@ntu.edu.sg

Widespread multidrug-resistance threatens to derail plans for the malaria eradication. Therapeutic failure has been reported in almost every clinically approved antimalarial, and novel antimalarials with unique mechanisms of action are of great need. However, this is hindered by the lack of target candidates for which therapies can be designed upon. We therefore aim to supplement the antimalarial drug discovery pipeline in both these aspects. We have identified several novel small molecules along with their putative intracellular targets. Compounds with distinct modes of action, a good selectivity index, being active against multiple stages of the parasite's life cycle, while also proving to have a low propensity for selection of resistance have been prioritized. Our studies have identified new chemical scaffolds for the development of the next antimalarial, but also potentially opened a new avenue in chemotherapeutic design against a critical enzyme of the parasite as well.

KL1

Targeting methyltransferases of SARS-CoV-2 and monkeypox virus

Jan Weber[a]

[a]*Institute of Organic Chemistry and Biochemistry of the Czech Academy of Sciences, Flemingovo náměstí 2, CZ-16000 Prague, Czech Republic*

E-mail: jan.weber@uochb.cas.cz

Many viral families, including coronaviruses and poxviruses, encode RNA methyltransferases (MTases) that catalyze methylation at the 5′ end of RNA to form a cap structure. This process is crucial for efficient translation of viral RNA and plays important roles in RNA stability and immune evasion. To mimic the host mRNA cap, SARS-CoV-2 utilizes its own capping enzymes, including two MTases: nsp14 (responsible for N7 methylation; cap-0 formation) and nsp16 (responsible for 2′-O methylation; cap-1 formation), both of which use S-adenosylmethionine as the methyl-group donor. In monkeypox virus (MPXV), the MTase VP39 catalyzes conversion of cap-0 to cap-1.

Here, I summarize efforts at our institute to target viral methyltransferases, specifically SARS-CoV-2 nsp14 MTase and MPXV VP39 MTase. A series of MTase inhibitors based on sinefungin was prepared, including compounds derived from 7-deazapurine and 7-substituted 7-deazapurine analogs of S-adenosyl-L-homocysteine, as well as a series of amides derived from adenosine-5′-carboxylic acid. These compounds exhibited low double-digit nanomolar activity in an in vitro nsp14 methyltransferase assay and submicromolar to double-digit nanomolar activity in the VP39 MTase assay.

The compounds were subsequently tested in cell cultures infected with SARS-CoV-2 and MPXV, and their contribution to immune activation was evaluated by measuring IRF3 phosphorylation using flow cytometry and by RT-qPCR analysis of interferon-stimulated genes. Structural analysis of methyltransferases from both viruses revealed high conservation of the catalytic pocket between MPXV VP39 and SARS-CoV-2 nsp16 MTases and, interestingly, a similar large hydrophobic cavity in MPXV VP39 and SARS-CoV-2 nsp14 MTases. These findings reinforce the possibility of developing pan-MTase inhibitors with a common mechanism of inhibition, even across evolutionarily distinct viruses such as MPXV and SARS-CoV-2.

KL2

A journey through viruses and public health

Lindomar Pena[a]

[a]*Department of Virology, Aggeu Magalhaes, Institute (IAM), Oswaldo Cruz Foundation (Fiocruz), Pernambuco, Recife, 50670-420, Brazil*

Emerging and re-emerging viral diseases continue to challenge public health systems worldwide, particularly in regions burdened by social inequities, environmental change, and vector-borne infections. Over the past decade, my research has focused on understanding viral emergence, improving diagnostic capacity, and developing translational approaches that connect basic virology with public health interventions.

This presentation highlights a scientific journey spanning epidemic preparedness, molecular diagnostics, environmental surveillance, and viral pathogenesis. To address the need for rapid outbreak response, we developed and validated innovative diagnostic platforms that enable local production of diagnostic reagents and research supplies, helping strengthen scientific autonomy and public health preparedness. In parallel, we have investigated the mechanisms of arboviral disease and identified novel antiviral strategies against Zika virus and related arboviruses, advancing the development of interventions to reduce viral replication and disease severity.

From epidemic investigation to diagnostic innovation and translational research, this body of work illustrates how virology can directly inform public health action. By integrating molecular biology, genomics, synthetic biology, environmental surveillance, and animal models, these efforts contribute to a One Health approach for improving preparedness and response to current and future viral threats.

KL3

Fumonisin B1, a common food toxin, induces cellular epigenetic changes that predispose to toxicity and disease

Anil A Chuturgoon[a]

[a]*Deputy Vice Chancellor of Research and Innovation, University of KwaZulu-Natal, Durban, 4000, South Africa*

E-mail: chutur@ukzn.ac.za

Fumonisin B1 (FB1) is a ubiquitous mycotoxin produced by *Fusarium* species that contaminate maize and other staple crops worldwide. Chronic dietary exposure is associated with oesophageal cancer, hepatocellular carcinoma and neural tube defects, yet classical toxicological mechanisms alone do not fully explain its long-term health impact. We explore how FB1 acts as an environmental epigenetic modifier that can reprogramme cellular regulation and predispose to toxicity and disease. The current data on FB1 occurrence in food chains is presented, with a focus on regions where maize is a dietary staple. The toxicity is due to the structural similarity of FB1 to sphingoid bases that disrupt sphingolipid metabolism, and this perturbation intersects with DNA methylation, histone modification and microRNA expression. Evidence from *in vitro*, animal and limited human studies indicates that FB1 exposure can induce locus specific and global epigenetic changes, alter gene expression in pathways related to apoptosis, inflammation and cell proliferation, and thereby create a "primed" cellular state that may enhance susceptibility to later insults. The emerging biomarkers of FB1 exposure such as some epigenetic signatures may be used for risk assessment, prevention and future translational research at the interface of toxicology, nutrition and precision medicine.

KL4

Single- or multitargeting 1,3,5-triazine ligands for serotonin 5-HT$_6$ receptor in search for innovative therapy of Alzheimer's disease

Jadwiga Handzlik[a]

[a]*Chair of Chemical Technology and Biotechnology of Drugs, Faculty of Pharmacy, Jagiellonian University Medical College, Medyczna 9, 30-688, Krakow, Poland*

E-mail: j.handzlik@uj.edu.pl

Alzheimer's disease (AD) is a neurodegenerative civilization problem, hard to treat due to highly complexed etiology. There are few AD drugs available on the pharmaceutical market with effectiveness limited to improve cognitive and memory processes, but unable to inhibit progressive neurodegeneration in AD patients. Current therapy using small-molecule drugs is primarily focused on regulating the cholinergic system, and among the recently FDA-approved biologics, the first (aducanumab) was withdrawn from therapeutic usage soon.

For over 20 years, the search for an effective and innovative AD drugs has been gathered around the 5-HT$_6$ serotonin receptor (5-HT$_6$R), which, due to its unique location limited to the CNS, and the phenomenon associated with the beneficial pro-cognitive effects of both agonists and antagonists, appears very promising in light of preclinical studies in animal models of AD. However, none of the seventeen 5-HT$_6$R antagonists, which reached the clinical trials, successfully passed I-III phases. Lines of evidence have indicated the following reasons of this failure: (i) too narrow chemical space of advanced antagonists (mainly indole/sulfone chemotype); (ii) unfavorable druglike parameters; (iii) single-target 5-HT$_6$R modulation insufficient for therapy of AD, a disease of such complexed etiology.

In response to these state-of-art, our team proposed an original non-indole and non-sulfone chemotype with a 1,3,5-triazine core (Fig. 1), which has been subjected to systematic rational modifications for last 10 years, yielding increasingly better effects in early preclinical studies, i.e. transitioning from a moderate 5-HT$_6$R single-target activity to potent and multitarget actions enhancing the potency of neuroprotection and inhibition of neurodegenerative processes typical for AD via appropriate enzymes and transcriptional factors [1].

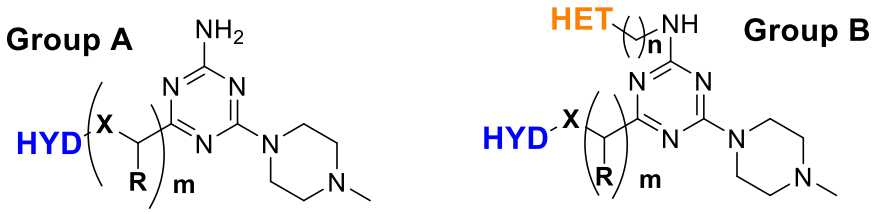

Figure 1: General structure of the investigated series. HET-heterocyclic; HYD -hydrophobic.

This lecture will outline path of the rational pharmacomodulation within a series of piperazine derivatives of 1,3,5-triazine (Fig. 1) with the use of comprehensive strategies, including computer-aided design, synthesis, and preliminary preclinical screening *in vitro* and *in vivo*, along with a discussion on the qualitative structure-activity relationships concluded with therapeutical perspectives for either single- or multitargeting profile involving 5-HT$_6$R as the main player [1,2].

Acknowledgement: *supported by National Science Centre Poland grant no.UMO-2023/51/B/NZ7/02177*

[1] P. Pyka et al. *J. Med. Chem.* **2024**, *67*, 1580-1610.
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KL5

Carbohydrate-mediated host recognition by microbial lectins: structural insights and inhibition strategies

Michaela Wimmerova[a,b]

[a]*National Centre for biomolecular Research, Faculty of Science, Masaryk University, 611 37, Brno, Czech Republic*
[b]*Central European Institute of Technology, Faculty of Science, Masaryk University, 625 00, Brno, Czech Republic*

E-mail: michaw@chemi.muni.cz

Lectins are non-immune carbohydrate-binding proteins that specifically recognize sugar structures without exhibiting catalytic activity toward their ligands. While some lectins participate in immune processes, they are not primary products of the immune response. Many microbial lectins bind carbohydrate moieties on host-cell glycoproteins and glycolipids, mediating adhesion to host tissues and mucosal surfaces and thereby acting as important virulence factors.

Our long-term research aims to identify, isolate, and characterize lectins from bacteria and fungi, with particular emphasis on pathogens affecting humans, plants, and insects to understand their involvement in the host recognition. Although lectins possess a variety of intriguing and potentially valuable properties, lectins from pathogenic organisms are primarily investigated as targets for disrupting host colonization and disease progression. Inhibition of lectin-mediated interactions may prevent infection or support therapeutic intervention. Accordingly, our research focuses on evaluating carbohydrate-based inhibitors of pathogen lectins using a range of experimental approaches, from simple hemagglutination and agglutination assays to advanced biophysical and cell-based methods.

KL6

Edible mushroom lectins and glycans promising therapeutic substances in human health

Seonghun Kim[a,b]

[a]*Jeonbuk Branch Institute, Korea Research Institute of Bioscience and Biotechnology (KRIBB), 181 Ipsin-gil Jeongeup 56212, Korea*
[b]*Department of Biosystems and Bioengineering, KRIBB School of Biotechnology, University of Science and Technology (UST), 217 Gajeong-ro, Daejeon 34113, Korea*

E-mail: seonghun@kribb.re.kr

Mushrooms are valuable resources of novel biopolymers such as lectins and polysaccharides for biotechnological and biomedical applications. Lectins are specific carbohydrate-binding proteins (GBPs) of non-immune origin. GBPs exhibit enormous diversity, complexity, and flexibility in their binding of glycans and glycoconjugates, which are found in dense and complex layers decorating the cell surfaces of organisms and are also involved in cellular and molecular interactions. Interestingly, more than 80% of reported lectins have been identified from mushroom species. Moreover, mushroom lectins exhibited binding specificity for complex glycan structures consisting of monosaccharides with various linkages and side chain modifications. In addition, mushroom polysaccharides are portentially prebiotic dietary fibers, which could promote human health by regulating gut microbiota, increasing the production of short-chain fatty acids, improving intestinal mucosal barrier. In this study, I present the brief introduction of mushroom lectins and an optimized purification procedure for core 1 O-linked glycan binding lectin from the fruiting body of *Hericium erinaceus* (mistakenly called *Hericium erinaceum*), which is an edible and medicinal mushroom found in East Asia (China, Korea, and Japan), as a model organism [1]. In addition, I also showed at least three different isolectins, HEL1, HEL2, and HEL3, in its fruiting body. Although these isolectins were similar molecular weights for a monomer type, these proteins displayed completely different glycan-binding specificities and affinities toward carbohydrate ligands: HEL1 and HEL2 (HEL2a and HEL2b) can bind fucosylated N-glycans and core 1 O-glycans, respectively [2,3]. The glycan-binding specificity of these lectins for detecting N-linked or O-linked glycans is comparable. Other HEL3 isolectins also can recognize higher branched polylactosamine (poly-LacNAc) comprising repeats of N-acetyllactosamine (Gal β(1,4)GlcNAc β(1,3)-R) units on glycoproteins among N-linked glycans [4]. These lectins can detect specific glycan epitopes for human disease biomarkers. The possible roles of diverse isolectins in the mushroom and its polysaccharides are discussed together with the mechanisms underlying the anti-proliferative activities and the health benefits, which may help to exploit these biomolecules as potential novel therapeutic agents via lectin-glycan interactions [5,6].

Acknowledgement: *This work was supported by Basic Science Research Program (NRF-2021R1A2C1005811) and through the National Research Foundation of Korea (NRF) and partially by KRIBB Research Initiative Program grant.*

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KL7

Galectin-8-targeting probes: small-molecule inhibitors versus PROTACs versus multivalent systems

Marko Anderluh,[a] Edvin Purić,[a] Sergej Pirkmajer,[b] Lara Smrdel,[a] Martina Gobec,[a] Hakon Leffler,[c] Ulf Nilsson[c]

[a]*Department of Pharmaceutical Chemistry and Department of Clinical Biochemistry, Faculty of Pharmacy, University of Ljubljana, 1000, Ljubljana, Slovenia*
[b]*Institute of Pathophysiology, Faculty of Medicine, University of Ljubljana, 1000, Ljubljana, Slovenia*
[c]*Centre for Molecular Protein Science, Department of Biochemistry and Structural Biology, and Centre for Analysis and Synthesis, Department of Chemistry, Lund University, Box 124, 221 00 Lund, Sweden*

E-mail: marko.anderluh@ffa.uni-lj.si

Galectin-8 (Gal-8), a tandem-repeat galectin, is involved in several diseases, including fibrosis, cancer, and heart disease, making it a target of interest for highly selective and potent Gal-8 inhibitors [1]. These inhibitors follow a rather traditional principle of occupying one of the carbohydrate binding sites of Gal-8, which directly inhibits the protein's function by a competitive binding mechanism. The current issue with these classical Gal-8 inhibitors is their rather modest potency, with inhibitory or binding constants that mostly reach the low micromolar concentration range, although our group just revealed inhibitors that reach high nanomolar Kd values [2].

Proteolysis targeting chimeras (PROTACs) have recently emerged as small-molecule modalities that hijack the cell's degradation pathway (ubiquitin–proteasome system) to selectively induce degradation of a specific protein of interest [3]. The current state-of-the-art in the design of PROTACs focuses mostly on intracellular proteins, yet Gal-8 (like many other galectins) exists both as an intracellular and an extracellular protein, which makes it a potential target for PROTACs-induced degradation. We have designed and synthesized a series of PROTACs designed to target Gal-8 and CRBN or VHL E3 ligases. These molecules were assayed for their Gal-8 and Gal-3 degradation in MD-MB-231 and HUVEC cell lines. Multivalent systems are regarded as a plausible option to achieve biologically relevant binding affinities and selectivities of lectin ligands [4]. To overcome the affinity issue, we have designed and synthesized several dendrons bearing multiple units of the starting monovalent Gal-8 inhibitor. PROTACs and multivalent Gal-8 inhibitors were further compared with classical small-molecule inhibitors by using a tube formation assay [5]. In this talk, we reveal for the first time such a comparison that led to successful Gal-8 inhibitors with potent anti-angiogenic effects.

Acknowledgement: *The financial support of this work from the European Union's Horizon2020 program under the Marie Skłodowska-Curie grant agreement No. 765581 (project PhD4GlycoDrug; www.phd4glycodrug.eu), EUTOPIA PhD Co-tutelle Programme grant, The Swedish Research Council (Grant no. 2020-03317) and the Slovenian Research Agency (Grants P1-0208 and J1-50026) is gratefully acknowledged.*

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KL8

Precision engineering of proteins in vitro, in live cells, and in vivo

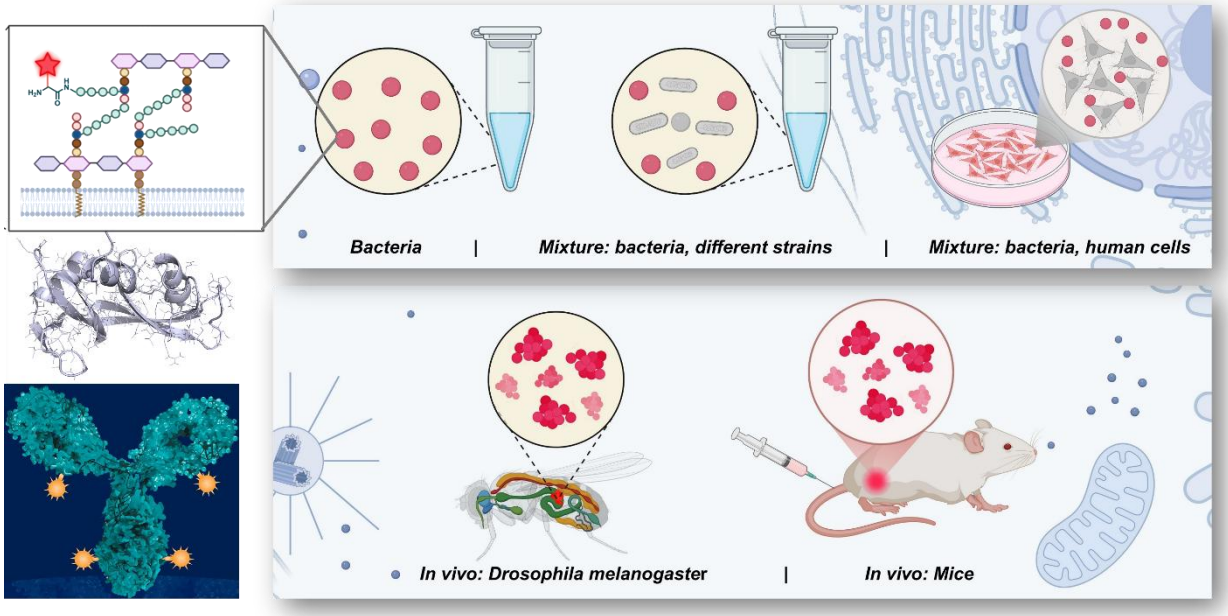
Vishal Rai[a]

[a]*Department of Chemistry, IISER Bhopal, India*

E-mail: vrai@iiserb.ac.in

Control over the selectivity of chemical modification of a protein presents a research question spanning chemistry, biology, and medicine. Regulated by multiple variables, it renders limited observables, making it challenging to perform hypothesis-driven research. In this presentation, I will discuss the principles of chemical technologies for precision engineering for proteins and antibodies [1-4].

Additionally, these insights can lead to technological advancements in homogeneous antibody-drug conjugates (ADCs) for targeted cancer chemotherapy and fluorophore conjugates (AFCs) for imaging-guided tumor surgery [4,5]. Lastly, I will provide a glimpse into how applying these principles in cellular or living systems can foster the development of chemistry for precision therapeutics [6].



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KL9

Synthesis and biological evaluation of heterocyclic scaffolds as potential agents against infectious diseases

Ronaldo Nascimento de Oliveira[a]

[a]*Department of Chemistry, Federal Rural University of Pernambuco, Recife-Brazil*

E-mail: ronaldo.noliveira@ufrpe.br

The discovery of New Chemical Entities (NCEs) with biological applications has emerged as a promising avenue in synthetic organic chemistry. Recently, we have focused on the design and synthesis of small-molecule derivatives containing azo-heterocyclic moieties, employing a variety of synthetic protocols [1-3]. This library of compounds was subsequently evaluated against several diseases, including tuberculosis, malaria, leishmaniasis, and viral infections such as arboviruses and SARS-CoV-2 [4-6]. The results revealed several promising lead candidates for future preclinical and clinical investigations.

***Acknowledgement**: CNPq, CAPES, FACEPE, CNPq-BRICS*

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KL10

The functional landscape of glycomimetics in translational glycobiology

Barbara Richichi[a]

[a]*Department of Chemistry "Ugo Schiff", University of Firenze, Via della Lastruccia 3-13, 50019 Sesto Fiorentino, Italy*

E-mail: barbara.richichi@unifi.it

Glycomimetics have clearly emerged as powerful tools for investigating and modulating glycan-mediated biological processes, advancing our understanding of glycans function while opening new perspectives in precision therapeutics [1]. Designed to replicate discrete sugar-based binding interactions, they enable glycoscientists to manipulate molecular recognition events and thereby elucidate how native glycans achieve their functional effects [2]. In this rapidly evolving field, the availability of efficient and versatile synthetic methodologies capable of readily accessing glycomimetics with highly diverse molecular architectures is key to fully exploit the potential of these compounds in translational glycobiology.

The use of glycals as dienophiles in inverse electron-demand [4+2] hetero-Diels–Alder (ihDA) reactions enable rapid access to structurally diverse glycomimetic scaffolds capable of mimicking different monosaccharide motifs [3]. The structural variability accessible through this strategy has allowed the exploration of multiple biological applications, ranging from inhibitors of tumor-associated glycosyltransferases for the precision "glycan-motif editing" of cancer glycocalyx to lectin binders for modulating dysregulated carbohydrate-mediated interactions [4-5]. Notably, our studies have also revealed that the functional potential of glycomimetics may extend beyond classical glycan mimicry, opening unexplored opportunities for the discovery of unconventional modes of molecular recognition, and providing early structural insights into key cancer-associated glycosyltransferases.

Acknowledgement: *European Union's Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Actions Grant Agreement n. 101119601 ("GLYCANDRUG")*

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KL11

Development of novel multistage antimalarials: lead optimization to clinical candidacy

Brijesh Rathi[a,b]

[a]*Laboratory For Translational Chemistry & Drug Discovery, Department of Chemistry, Hansraj College, University of Delhi, Delhi- 110007, India*
[b]*HG Khorana Centre For Chemical Biology, Department of Chemistry, Hansraj College, University of Delhi, Delhi- 110007, India*

E-mail: brijeshrathi@hrc.du.ac.in

Malaria remains one of the most devastating infectious diseases globally, claiming over 600,000 lives annually. The emergence of drug-resistant Plasmodium strains underscores the urgent need for novel, multistage-active antimalarial agents. Multistage antimalarials are expected to broaden the therapeutic scope and also counteract the resistance of the frontline therapeutics. We pursued a rational, pharmacophore-guided approach to antiparasitic drug discovery, integrating green synthetic protocols, computational docking, and cross-disciplinary biological evaluation. A remarkable low nanomolar inhibitory activity of the compounds (*i.e.*, piperazine analogs) against the asexual blood stage was observed on *Pf*3D7 and artemisinin-resistant field strains. Likewise, our compounds displayed a strong inhibition against the *P. berghei* liver stage with nanomolar IC_{50} values in culture and in the mice model. A few compounds were highly effective on the cultured mixed gametocyte stages resulted at low nanomolar concentrations. Compounds were administered parallelly with the gametocyte-infected blood, and the results were measured as the % reduction of oocysts in the mosquito midgut. Our results suggested that mosquito fed with compound perceived a significant decline in the number of oocysts formed in the midgut of mosquito. Significant reduction in the development of the ookinete (ex-vivo) and gametocyte stages leads to transmission blocking efficacy. Toxicity studies in mice indicated a safety margin in the tissues of different organs. Subacute toxicity at a dose of >400 mg/Kg was assessed in the mice that supported a normal functioning of liver and kidney organs as well, no apparent toxicity in mammalian cells combined with favorable pharmacokinetics evaluated in mice. The lead molecule is currently being tested in primates.

Acknowledgement: *The authors acknowledge the financial support received from ANRF, Government of India (CRD/2022/000580) & Department of Biotechnology, Government of India (BT/PR54322/BMS2/156/92/2024).*

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KL12

Translational research in HIV/AIDS and its role in changing clinical practices

Pulin Kumar Gupta[a]

[a]*ABVIMS and Dr Ram Manohar Lohia Hospital, 110001, New Delhi, India*

E-mail: guptapulin@yahoo.com

HIV/AIDS remains a major global health challenge despite substantial advances in antiretroviral therapy. Contemporary therapeutic strategies increasingly integrate translational research approaches to bridge molecular discoveries with clinical application, aiming to improve viral suppression, immune restoration, and long-term patient outcomes. Emerging interventions such as broadly neutralizing antibodies, latency-reversing agents, gene-editing technologies, therapeutic vaccines, and long-acting antiretroviral formulations are reshaping the future landscape of HIV management. Translational medicine has enabled deeper understanding of viral reservoirs, immune dysregulation, and mechanisms of drug resistance, facilitating the development of personalized and precision-based therapeutic models.

Recent innovations emphasize not only viral control but also functional cure strategies and reduction of treatment-associated toxicities. Integration of biomarker-driven diagnostics and pharmacogenomics further enhances individualized care and therapeutic monitoring. These advancements hold significant implications for clinical management, including improved adherence through extended-release therapies, reduced transmission rates, and enhanced quality of life among affected individuals. Furthermore, interdisciplinary translational research strengthens the connection between laboratory science, clinical trials, and public health implementation, accelerating the adaptation of novel therapies into routine practice.

Overall, evolving therapeutic strategies grounded in translational research represent a transformative shift in HIV/AIDS management, offering promising opportunities for durable remission, optimized clinical outcomes, and advancement toward global disease control objectives.

Abstracts of oral presentations

OL1

Targeting a unique mRNA decapping enzyme for trypanosomatid infectious disease drug discovery

Emmanuel Agbebi,[a] Maria Grechnikova,[a] Leticia Pereira,[b] Dawid Dzadz,[c] Alexia Achilles Amaral,[b] Paula Castaneda Londono,[b] Natalia Karolak,[c] Marcin Warmiński,[d] Marcelina Bednarczyk,[d,e] Jacek Jemielity,[e] Pavel Šácha,[f] Joanna Kowalska,[d] Maria Gorna,[c] Susanne Kramer,[b] Martin Zoltner[a]

[a]*Department of Parasitology, Charles University in Prague, BIOCEV, Prague, Czech Republic*
[b]*Biocenter, University of Würzburg, Würzburg, Germany*
[c]*Structural Biology Group, Biological and Chemical Research Centre, Department of Chemistry, University of Warsaw, Warsaw, Poland*
[d]*Division of Biophysics, Faculty of Physics, University of Warsaw, Warsaw, Poland*
[e]*Centre of New Technologies, University of Warsaw, Warsaw, Poland*
[f]*Institute of Organic Chemistry and Biochemistry of the Czech Academy of Sciences, Prague, Czech Republic*

Trypanosomatids encode no homologues of canonical decapping enzymes, but employ the ApaH-like phosphatase ALPH1, belonging to a phosphatase family absent in mammalian systems, for the essential process of mRNA decapping. We have shown that *T. brucei* ALPH1 functions within a decapping complex and thorough characterisation, both biochemically and in the cellular context, renders ALPH1 a robust drug target. We set out to conduct a screening campaign to identify inhibitors with the potential to become highly selective candidate drugs for trypanosomatid caused diseases, including African sleeping sickness, Chagas Disease and the leishmaniases. We have developed a robust assay strategy to monitor inhibition of ALPH1 activity, relying on the quantification of ADP liberated from a dinucleotide cap analog. Here we present novel mechanistic insights into the trypanosome decapping complex and report the outcome of our pilot screen encompassing 12760 small molecules.

OL2

Functional dynamics in binding of a cell-wall analogue peptide to the glycopeptide antibiotic eremomycin: a ^{15}N NMR relaxation study

Gyula Batta,[a] Réka Erdei[a]

[a]*University of Debrecen, 4032, Debrecen, Hungary*

E-mail: batta@unideb.hu

Glycopeptide antibiotics are invaluable for the treatment of severe Gram-positive bacterial infections however, increasing resistance needs a better understanding of their mode of action. We investigated the thermodynamic aspects of ligand binding to the glycopeptide antibiotic eremomycin [1-5] using ^{15}N NMR relaxation studies, concerning the role of conformational entropy. By quantifying the S^2 backbone NH order parameters in the free and ligand-bound states, we found that binding of the cell wall analogue peptide NAc-D-Ala induces a local increase in the internal dynamics at the binding site of the antibiotic, giving an entropic gain upon binding. We also observed, that solvent (H_2O) accessibility around the binding site is reduced. These observations provide an experimental support for the hypothesis that entropic compensation arising from enhanced internal motion contributes to the cooperativity between ligand binding and eremomycin dimerization. Furthermore, cross-correlated ^{15}N CSA/DD relaxation experiments confirm that the cis configuration of the peptide bond at residue 6 is conserved. Together, these results suggest that enhanced conformational entropy plays a role in the antibiotic-ligand interaction.

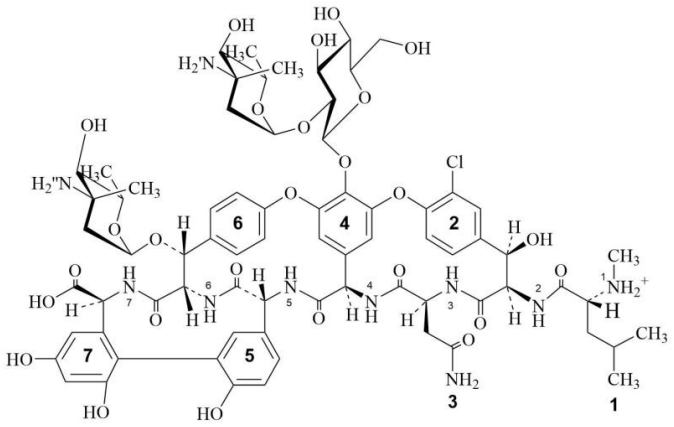

Figure 1: The structure of eremomycin

Acknowledgement: *This research was funded by the Hungarian National Research, Development and Innovation Office, grant number NKFI-1, ADVANCED_25, 152435. Also was supported by the University of Debrecen Scientific Research Bridging Fund (DETKA). This work was supported by the Gedeon Richter Talentum Foundation, within the framework of the Excellence PhD Scholarship Program.*

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OL3

Synthesis and antimalarial activity of water-soluble cannabinoids

Ferenc Dániel Petróczi,[a,b,c] Angéla Tótik,[a] Amir Foroutan,[a] Anikó Borbás,[a] Pál Herczegh,[a,d] Brijesh Rathi,[e] Himanshi Sharma,[e] Ilona Bakai-Bereczki,[a,d]

[a]*University of Debrecen, Department of Pharmaceutical Chemistry, 4032, Debrecen, Hungary*
[b]*University of Debrecen, Doctoral School of Pharmaceutical Sciences, 4032, Debrecen, Hungary*
[c]*GlycOptim Kft., 4032, Debrecen, Hungary*
[d]*University of Debrecen, HUN-REN-DE Pharmamodul Research Group, 4032, Debrecen, Hungary*
[e]*University of Delhi, 110007, Delhi, India*

E-mail: petroczi.f.daniel@pharm.unideb.hu, bereczki.ilona@pharm.unideb.hu

Cannabidiol (CBD) and cannabigerol (CBG) are non-psychoactive phytocannabinoids that can be found in *Cannabis sativa*. They interact with cannabinoid receptors (CB_1, CB_2). They can be potentially applied in nervous system disorders and they possess antioxidant, anti-inflammatory, cardioprotective, antiviral and antibacterial effects. There are only a few examples of systematic synthetic modifications in the scientific literature, therefore, we aimed to chemically modify these cannabinoids to improve their pharmacodynamic and pharmacokinetic properties [1-3]. We alkylated the phenolic hydroxyl groups of the two compounds with various amine derivatives and subsequently formed salts from some of these derivatives. We have successfully synthesized mono- and disubstituted derivatives and have optimized the reaction conditions. The synthesized derivatives, as well as the salts formed from them are stable, water-soluble, and easy to handle, and their purity is sufficient for biological and blood–brain barrier studies, which are in progress. Some compounds exhibited outstanding antimalarial activity.

Acknowledgement: *This research was supported by the National Research, Development and Innovation Office of Hungary FK 142315, the KDP-2023 Program of the Ministry for Culture and Innovation from the Source of the National Research, Development and Innovation Fund. This research was also supported by „Debrecen Venture Catapult Program" EFOP-3.6.1-16-2016-00022 and the PhD Excellence Scholarship from the Count István Tisza Foundation for the University of Debrecen.*

MINISTRY OF INNOVATION AND TECHNOLOGY / NATIONAL RESEARCH, DEVELOPMENT AND INNOVATION OFFICE HUNGARY / PROJECT FINANCED FROM THE NRDI FUND

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OL4

Impact of sacubitril/valsartan therapy on left ventricular reverse remodelling and clinical outcomes in patients with CRT nonresponders and HFrEF patients without CRT indication

Krisztina Mária Szabó,[a] Zoltán Csanádi[a]

[a]*Department of Cardiology and Cardiac Surgery, Clinical Center, University of Debrecen, 4032, Debrecen, Hungary*

E-mail: dr.szabo.krisztina.maria@med.unideb.hu

Introduction: Non-responders to Cardiac Resynchronization Therapy (CRT-NR) have poor prognosis. Sacubitril/valsartan (SV) treatment improved the outcome of heart failure (HF) patients with reduced left ventricular ejection fraction (HFrEF) in randomized trials with limited data on the specific cohort of CRT-NRs. Herein we compared echocardiographic and biomarker changes as well as hospitalization and mortality in CRT-NR patients treated with versus without SV, and in HFrEF patients on SV therapy.

Methods:CRT-NR patients initiated on SV (Group I:70); CRT-NR patients kept on angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEi/ARB; Group II:70), and HFrEF patients (without CRT) initiated on SV (Group III:135) were identified in a prospective HF registry. CRT-NR was defined as <10% improvement in left ventricular ejection fraction (LV EF) 6 months after the implantation. Echocardiographic parameters and N terminal pro-B-type Natriuretic Peptide (NT-proBNP) levels at baseline and at 6-month follow-up as well as mortality and hospitalizations for HF at 24-month follow-up were compared.

Results: 275 patients were included. After a follow-up of 7.54±1.8 months (mean±standard deviation (SD), LV EF (%) increased significantly ($p<0.001$) in Group I and in Group III. The levels of NT-proBNP (pg/mL) decreased in Group I (from 2058.86 [1041.07-4502.51] to 1121.55 [545-2541];$p<0.001$), and in Group III (from 2223.35 [1233.03-4795.96] to1123.09 [500.38-2651.27]; $p<0.001$). No significant changes were demonstrated either in LV EF or in NT-proBNP in Group II. Over a median follow-up of 22 months, all-cause mortality was observed in 14 out of 70 patients (20%) in Group I, 19 out of 70 patients (27.1%) in Group II, and 27 out of 135 patients (20%) in Group III [HR 0.55, 95% CI (0.27-1.11); $p = 0.06$]. HF hospitalization occurred in 19 out of 70 patients (27.1%) in Group I, 38 out of 70 patients (54.2%) in Group II, and 36 out of 135 patients (26.6%) in Group III [HR 0.35,95% CI (0.20-0.62); $p < 0.01$].

Conclusion: SV therapy induced reverse remodeling at a similar magnitude evidenced by significant improvements in echocardiographic parameters and in NT-proBNP levels in CRT-NR and in HFrEF patients without resynchronization. It also demonstrated significant improvement in hospitalization rates and a trend for improved mortality in both patient cohorts.

Acknowledgement: *The research and preparation of this publication were supported by Project No. TKP2021-EGA-18, financed from the National Research, Development and Innovation Fund of the Ministry of Culture and Innovation under the TKP2021-EGA funding scheme.*

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OL5

Clostridioides difficile: an emerging global pathogen and a model organism for one health approaches to human disease

Ravi Durvasula[a]

[a]*Chair of Infectious Diseases, Professor of Medicine, Mayo Clinic Florida*

E-mail: Durvasula.Ravi@mayo.edu

Infections due to Clostridioides difficile threaten hospitalized patients across the globe. Though epidemiological investigations of C difficile are more abundant in North America and Europe, emergence of this infection in many other countries is ongoing. In the US alone, C difficile infection accounts for an additional $9 billion in annual healthcare costs. Traditionally, C difficile has been regarded as a hospital-acquired infection, often due to antecedent antibiotic use or immunosuppression. Though re-activation of toxigenic forms of this bacterium in colonized hosts due to antibiotic-mediated depletion of protective gut flora remains a leading concern, there is growing evidence of zoonotic and environmental reservoirs of C difficile infection. Furthermore, rapid emergence of mutated strains that exhibit both drug resistance and enhanced toxin production poses grave threats to health systems.

This presentation will provide an overview of the global C difficile epidemic and will address:

(1) Current epidemiology of C difficile
(2) Pathogenesis of C difficile at the molecular level
(3) Zoonotic reservoirs and one health implications
(4) Current and evolving therapeutics
(5) Prospects for vaccine development against C difficile

OL6

Sweet carriers: cyclodextrin polymers in the design of novel RNA delivery systems

Virág Dajka,[a] Péter Magyar,[a] Ildikó Bácskay,[b] Ferenc Fenyvesi,[a] Ágnes Rusznyák[a]

[a]*Department of Molecuar and Nanopharmaceutics, University of Debrecen, H4032 Debrecen, Hungary*
[b]*Department of Pharmaceutical Technology, University of Debrecen, H4032 Debrecen, Hungary*

E-mail: rusznyak.agnes@euipar.unideb.hu

Nowadays, RNA-based therapies play an increasingly important role in the treatment of various diseases. siRNA is mainly used in the maintenance of different genetic diseases, while the mRNA also used in the development of vaccines. Due to the large molecular size and polyanionic nature of RNA, the intracellular delivery of these molecules are difficult [1]. To solve this problem several delivery systems are available or under development, which are usually based on liposomes and cationic polymers, such like cyclodextrin polymers [2]. In the present study we aimed to investigate and to compare the siRNA and mRNA carrying capacity of a cationic cyclodextrin polymer (Q polymer) and the polyethylenimine (P polymer), which is used in the practice.

The cytotoxicity effect of the applied polymers was examined using the MTT method. The siRNA and mRNA polyplexes were formulated in different mass ratios (MR). The formulated polyplexes were characterized based on their size distribution using dynamic light scattering (DLS) and their zeta potential. In the case of siRNA polyplexes their cellular internalization was investigated by confocal microscopy. The intracellular effect of these delivery systems was investigated via the expression of GAPDH (siRNA) green fluorescent protein (mRNA) by fluorescence microscopy and flow cytometry.

The P polymer was more cytotoxic than the cationic cyclodextrin polymer. According to the DLS and zeta potential measurements both polymer were able to form polyplexes with siRNA and mRNA, but based on the gel electrophoresis, the cyclodextrin polymer is able to form a stronger polyplex with mRNA molecule. Polyplexes formulated with Q polymer were able to enter the cells, while these formulated with P polymer were bound to the cell membrane. Polyplexes were influenced both the GAPDH and green fluorescent protein (GFP) expression, but the increasing concentration of P polymer was cytotoxic.

In summary, we have successfully formulated cyclodextrin polymer-based RNA delivery systems. Polyplexes formulated with different polymers showed different cellular internalization. The formulated polyplexes are able to influence the expression of different proteins and the cationic cyclodextrin polymer is more suitable for gene or protein expression than for gene silencing.

Acknowledgement*: Project no. TKP2021-EGA-18 has been implemented with the support provided by the Ministry of Culture and Innovation of Hungary from the National Research, Development and Innovation Fund, financed under the TKP2021-EGA funding scheme.*

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OL7

TT-232, a somatostatin analogue levels in blood and cerebrospinal fluid after various administrations

Miklós Vecsernyés,[a] Attila Kiss,[b] István Lekli[c]

[a]*Department of Pharmaceutical Surveillance and Economics, Faculty of Pharmacy, University of Debrecen*
[b]*Department of Organic Chemistry, Faculty of Science and Technology, University of Debrecen*
[c]*Department Pharmacodynamics, Faculty of Pharmacy, University of Debrecen H-4028 Egyetem square 1, Debrecen, Hungary*

E-mail: vecsernyes.miklos@pharm.unideb.hu

TT-232 is a structurally unique somatostatin analogue with selective SSTR4 activation. It has been shown to confer potent antitumor and anti-inflammatory effects. Its mechanisms involve inhibition of proliferative signaling, induction of apoptosis via PKM2 interaction, and modulation of pain and inflammation pathways. Early clinical trials indicate good tolerability, and ongoing studies are exploring its efficacy in cancer and chronic inflammatory diseases. Here we aimed to investigate the level of TT-232 in blood and cerebrospinal fluid after and iv and ip administration. In order to validate the results, we have obtained TT-232d8 molecule and the experiments were repeated with TT-232 and TT-232d8 respectively. Following TT-232 administration to the rats, blood samples were collected at 5, 30, 60, and 120 minutes; cerebrospinal fluid (CSF) was also obtained at the final time point. After sampling, the blood was centrifuged and acetonitrile was added to the serum in a 1:2 ratio to precipitate the proteins. Acetonitrile was also added to the CSF samples in a 1:2 ratio. Following centrifugation, the samples were analyzed using LC-MS. As a separation method, ACN:water gradient elution was used on a conventional C18 stationary phase starting from 10% (v/v) of ACN in water to 100% ACN. LCMS experiments were done using MSMS measurement mode to tt232d8 molecular ion (955.6 m/z). The product ion spectra were detected. We have optimized the LCMS method for TT-232 detection. Furthermore, we were able to detect TT-232 in the blood and CSF respectively ip and iv administration.

OL8

The mechanosensitive Piezo1 channels contribute to the arterial medial calcification

László Szabó,[a,b] Andrea Tóth,[c] Mónika Gönczi,[a,b] Dávid Máté Csiki,[c] Csaba Tóth,[d] Ildikó Balatoni,[e] Viktória Jeney,[c] László Csernoch,[a,b] Beatrix Dienes[a,b]

[a]*Department of Physiology, Faculty of Medicine, University of Debrecen, Debrecen, Hungary.*
[b]*HUN-REN-DE Cell Physiology Research Group, University of Debrecen, Debrecen, Hungary.*
[c]*MTA-DE Lendület Vascular Pathophysiology Research Group, Research Centre for Molecular Medicine, Faculty of Medicine, University of Debrecen, Debrecen, Hungary.*
[d]*Department of Surgery, Faculty of Medicine, University of Debrecen, Debrecen, Hungary.*
[e]*Clinical Center, University of Debrecen, Debrecen, Hungary.*

E-mail: dienes.beatrix@med.unideb.hu

Vascular calcification (VC) has been linked to numerous cardiovascular diseases as well as chronic kidney disease. The role of smooth muscle cells (SMCs) in VC has been extensively studied, as has the role of intracellular Ca^{2+} in the regulation of SMC function. It has been suggested that increased intracellular calcium concentrations ($[Ca^{2+}]_i$) in vascular SMCs stimulate VC. However, the contribution of non-selective Piezo1 mechanoreceptive cation channels to the rise in $[Ca^{2+}]_i$, and consequently to the VC process, has never been investigated. In this work, we demonstrate the fundamental contribution of Piezo1 channels to arterial medial calcification. We confirmed the presence of Piezo1 using immunohistochemical methods on human aortic smooth muscle cell samples. Quantitative PCR and Western blot analysis confirmed the expression of the channel in the human aortic smooth muscle cell line (HAoSMC). Functional measurements were performed on HAoSMC under control and calcification conditions. Calcification was induced by supplementing the culture medium with inorganic phosphate (1.5 mmol/L, pH 7.4) and calcium ($CaCl_2$, 0.6 mmol/L) for 7 days. We measured $[Ca^{2+}]_i$ using the fluorescent dye Fura-2 following stimulation of Piezo1 channels (with hypoosmolarity or Yoda1) and detected significantly higher calcium transients in calcified HAoSMCs than in control HAoSMCs. Expression of the mechanoreceptive Piezo1 channel is upregulated in calcified arterial SMCs, resulting in greater calcium influx upon stimulation. Activation of the channel by Yoda1 (10 μmol/L) enhanced calcification of HAoSMCs, whereas Dooku1, which antagonizes the effect of Yoda1, reduced this enhancement. The application of Dooku1 alone inhibited calcification. Downregulation of Piezo1 using siRNA suppressed the calcification induced by Yoda1 under calcification conditions. Our results demonstrate the key role of Piezo1 channels in arterial medial calcification.

OL9

Effect of some popular natural active ingredients of dietary supplements on the endothelial function of isolated rat aorta

Rudolf Gesztelyi,[a] Rita Kiss,[a] Bela Juhasz[a]

[a]*Department of Pharmacology and Pharmacotherapy, Faculty of Medicine, University of Debrecen, H-4032 Debrecen, Hungary*

E-mail: gesztelyi.rudolf@med.unideb.hu

Agonists of muscarinic and P2Y purinergic receptors evoke NO-mediated relaxation in arteries. Since this response requires functionally intact endothelium, it is a generally accepted indicator of endothelial function. Lutein, zeaxanthin and pterostilbene are popular phytopharmaceuticals found in many dietary supplements. Their widespread use justifies the need to explore their potential effects on endothelial function, which latter plays an important role in the regulation of blood pressure and thus in several diseases causing major public health concerns (e.g., stroke, myocardial infarction and heart failure).

In one of two studies from our laboratory, 3 groups of 18-week-old Sprague Dawley rats were treated with 3 mg/kg/day lutein, or 5 mg/kg/day pterostilbene, or their vehicle, via gavage for 5 weeks. In the other study using 8-10-week-old Sprague Dawley rats, 1 group received only conventional chow for 80 weeks, while 2 other groups were additionally fed 5-6.5 g/animal/day maize for 80 weeks, which maize contained approximately 60 µg/g lutein, furthermore 18 µg/g and 26 µg/g zeaxanthin, respectively. Following the in vivo treatment periods, the distal portion of the thoracic aorta was isolated from the animals in both studies, from which 2-3 mm wide rings were cut. Each aortic ring was mounted under 8 mN resting tension in a vertical organ bath filled with Krebs solution (36 °C, pH = 7.4) gassed with carbogen (95% O_2, 5% CO_2). The contractile force of the aortic rings was measured. After their mechanical activity had stabilized, concentration-effect (E/c) curves with acetylcholine and ATP (separated by a long washout period) were generated on the rings, following a precontraction evoked by 20 nmol/L norepinephrine.

Each in vivo phytopharmacological treatment shifted the acetylcholine E/c curve in the same direction as the corresponding ATP E/c curve. Lutein, both alone and in combination with zeaxanthin, reduced the relaxation response, i.e. impaired the endothelial function (this effect of lutein was not statistically significant when used alone or together with 18 µg/g zeaxanthin, but it was significant when used in combination with 26 µg/g zeaxanthin). In contrast, pterostilbene increased the relaxation response, i.e. improved the endothelial function (non-significantly when compared to the control, but significantly when compared to lutein).

Our results highlight the need for extensive investigations of the active ingredients of dietary supplements, even if they have been proven to exert beneficial effects on certain conditions and are therefore considered well-established compounds.

Keywords: maize, lutein, pterostilbene, zeaxanthin, aorta, endothelial function, ex vivo, rat

Acknowledgement: *Supported by EKÖP-24-4-I-DE-279, 2020-1.1.2-PIACI-KFI-2020-00064, TKP2021-EGA-18.*

OL10

From poorly structured clinical patient records to analyzable variables: challenges and solutions

Imre Bakos,[a] László Kardos,[a] Mohamed Mahdi,[a] Beáta Lénárt,[a] Zsófia Nábrádi,[a] István Várkonyi[a]

[a]*Clinical Department of Infectious Diseases, University of Debrecen Clinical Center, H-4032, Debrecen, Hungary*

E-mail: dr.kardos.laszlo@med.unideb.hu

In the framework of a major research project analyzing digital medical data generated through outpatient and inpatient care at the University of Debrecen Clinical Center (UDCC) for patients affected by the COVID-19 pandemic, we faced unique challenges rooted in an immense amount of information technically existing but being inaccessible for statistical processing which generally requires data arranged in variables, i.e., a columnar representation of each of several properties, rather than buried in human-generated free text. To overcome this, we developed a software solution to facilitate the large-scale conversion of unstructured textual information into variables, with an emphasis on verification based on true semantic comprehension by human experts.

The data of all patients who received care for COVID at the UDCC in the period 2020-01-01 through 2023-04-03 were extracted by data specialists at UDCC's Health Finance and Controlling Directorate from the medical system in use at UDCC. They came in separate files for demographic data, inpatient admissions, outpatient service events, inpatient diagnostic codes (ICD-10), outpatient diagnostic codes, inpatient interventions, inpatient discharge summary full texts, outpatient sheet full texts, and laboratory findings, all linkable through person and case identifiers. First, a unique list of all words found in the full text variables was extracted. The procedure of finding relevant information in the full texts started by defining a keyword, e.g., if the objective were to create an indicator variable on whether the patient had received remdesivir, the keyword would be "remdesivir". From the word list, items were scored on similarity to the keyword (Levenshtein distance) to identify spelling and mistyped variant candidates, which were verified by a human expert. All verified variants were then searched for in the full texts, and text snippets made up of any hit with its context (~50 surrounding characters on either side), plus patient and case identifiers, were collected in a spreadsheet file. Finally, human experts manually checked each entry in the spreadsheet file and set the value of the target indicator variable accordingly. In the very rare instances when the extracted context was insufficient for judgment, the full text of the discharge summary or outpatient sheet was retrieved for thorough reading. Spread across a dozen or so human experts, the processing of a mass of medical documents in the magnitude of tens of thousands was observed to be achievable within realistic timelines measured in single-digit net working hours for each expert.

We concluded that this system immensely reduces the processing time required as compared to raw human reading of documents while preserving the role of human expert opinion rather than outsourcing the task to a fully automated procedure with known potential problems such as high false positive and negative rates and reliance on a "black box" type operation.

Acknowledgement: *The authors wish to thank Director István Ludman and his staff at the Health Finance and Controlling Directorate for their valuable contributions to this research.*

OL11

Evolutionary adaptation and host–virus dynamics in emerging RNA viruses

Mansi Verma[a]

[a]*Department of Zoology, Hansraj College, University of Delhi, Delhi 110007, India*

E-mail: mansiverma@hrc.du.ac.in

RNA viruses such as Influenza, SARS-CoV2 and Dengue viruses are rapidly evolving due to elevated mutation rates, recombination, reassortment and continuous host adaptation [1]. These evolutionary mechanisms contribute not only to zoonotic transmission events but also in immune evasion and the emergence of epidemic and pandemic lineages [2, 3]. Therefore, understanding such evolutionary events requires extensive viral genome analyses critical for virus-host interactions and evolutionary dynamics. Comparative studies of riboviral genomes have highlighted a significant variation in evolutionary rates, influencing viral pathogenicity, transmission potential and host specificity. Additionally, the study of mutational hotspots, CpG dinucleotide suppression and codon usage adaptation offers deeper insights into viral adaptation and host immune mechanisms.

In our attempts, we have conducted several comparative genomics studies on influenza Virus, Dengue Virus [4, 5] and SARS-CoV-2 [6,7], and a plethora of information is obtained using these genomes, highlighting the importance of comparative studies.

Several novel vaccine candidates and repurposed drugs were found using such studies. Understanding these molecular evolutionary mechanisms is crucial for predicting zoonotic emergence and improving future antiviral and vaccine development strategies.

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OL12

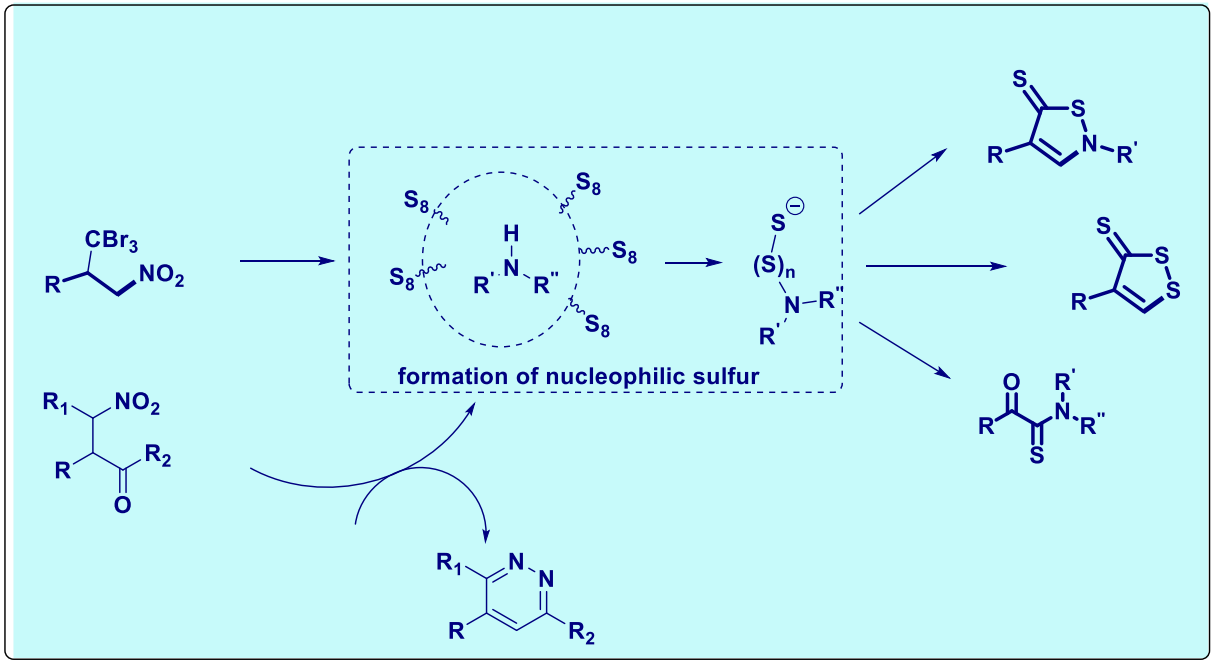
Umpolung reactivity of nitromethyl group for the selective synthesis of -S and -N heterocyclics

Ankush Gupta,[a] Gururaja Guddeangadi Nagraja,[b] Brijesh Rathi[a]

[a]*Laboratory for Translational Chemistry and Drug Discovery, Department of Chemistry, Hansraj College, University of Delhi, Delhi-110007*
[b]*School of Chemical Sciences, Central University of Gujarat, Gandhinagar, Gujarat-382030*

E-mail: ankushorganic@hrc.du.ac.in

Herein, we report the selective routes for the synthesis of Isothiazoles-thione, dithiols-thione, and ketothioamide and Pyridazines via unique umpolung reactivity of the nitromethyl group in β–tribrobromoderivatives Adduct of nitroalkene and γ- nitro ketone. The presented protocol describes product formation via regioselective, chemodivergent pathways by tuning solvent and temperature.



Keywords: Umpolung. amines, elemental sulfur, organosulfur molecules

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OL13

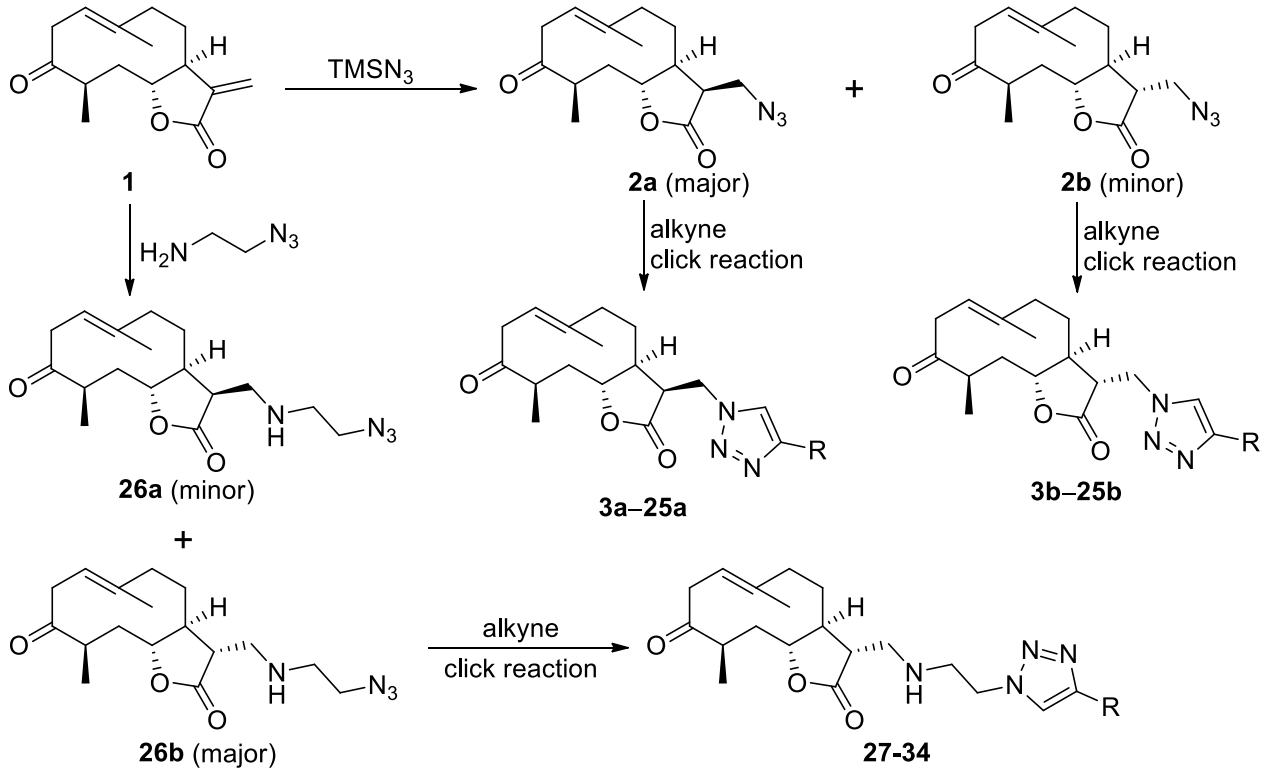
Synthesis of argolide-derived conjugates by “Click” chemistry

Nguyen Thi Cam Tu,[a] Attila Márió Remete,[a] Zsolt Szakonyi,[a] Sergazy M. Adekenov,[c] Tam Minh Le[a,b]

[a]Institute of Pharmaceutical Chemistry, University of Szeged, Eötvös u. 6, H-6720 Szeged, Hungary
[b]HUN-REN–SZTE Stereochemistry Research Group, University of Szeged, Eötvös u. 6, H-6720 Szeged, Hungary
[c]JSC Research and Production Center “Phytochemistry”, Karaganda 100009, Kazakhstan

E-mail: ntctupharmacy@gmail.com

Sesquiterpene lactones and their derivatives exhibit various biological activities, such as antifungal, antimicrobial, immunomodulatory, anticancer, and cytotoxic properties due to the α-methylene-γ-lactone moiety [1,2]. The germacranolide, argolide, isolated from the aerial parts of *Artemisia glabella* Kar. et Kir. [3], was used as the starting material for the preparation of 1,4-disubstituted-1,2,3-triazoles conjugates. Initially, the Michael addition of argolide with $TMSN_3$ and 2-azidoethylamine resulted in the corresponding azides **2a–b** and **26a–b**. Subsequently, all these azides were subjected to the Huisgen 1,3-dipolar cycloaddition (click reaction) with different terminal alkynes [4] providing the target products: **3–25** and **27–34**, respectively.



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OL14

Cardioprotective potential of fluorinated cannabinoids in H9c2 cells

Richárd Kajtár,[a] Kitti Szőke,[b] Alexandra Gyöngyösi,[b] Simon Eskeif,[a] Adina Fésüs,[b] Éva Sípos,[b] Dániel Ferenc Pertóczi,[c] Ilona Bakai-Bereczki,[c] Anikó Borbás,[c] Ferenc Papp,[d] Russo Teklu Teshome,[d] István Lekli[b]

[a]*Department of Pharmacodynamics, Faculty of Pharmacy, Doctoral School of Pharmaceutical Sciences, University of Debrecen, 4002, Debrecen, Hungary*
[b]*Department of Pharmacodynamics, Faculty of Pharmacy, University of Debrecen, 4002, Debrecen, Hungary*
[c]*Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Debrecen, 4032, Debrecen, Hungary*
[d]*Department of Biophysics and Cell Biology, Faculty of Medicine, University of Debrecen, 4032, Debrecen, Hungary*

E-mail: kajtar.richard@pharm.unideb.hu

In the last two decades cannabinoids have been the focus of extensive research due to their versatile pharmacological profile. Cannabidiol (CBD) is one of the most abundant molecules in *Cannabis sativa*, because of this, it is one of the most extensively studied phytocannabinoids. However, the literature is quite limited about synthetically modified cannabinoids. We aimed to investigate the effect of some novel CBD derivatives primarily evaluating their cardioprotective effect against different stress factors. Our collaborators chose fluorination as a modification on the basic CBD molecule due to such as modifications have been shown to drastically improve the efficacy of the original molecule in several medications. We assessed the cytotoxicity of these derivatives using an MTT assay on H9c2 rat cardiomyocytes and evaluated their ability to protect cells from H_2O_2-induced oxidative stress. Antioxidant capacity was measured using FRAP, ORAC, ABTS, and CUPRAC assays. Additionally cardioprotective potential was tested against doxorubicin (known anticancer drug with serious cardiotoxic side effect) using a pre-treatment protocol followed by exposure to the cardiotoxic agent. Subsequently we investigated the background of the protective effect, we carried out multiple western blot analyses under different conditions in order to evaluate the change in the endogenous antioxidant system. Furthermore one of our collaborator also evaluated the effects of the compounds on h-ERG channels. Regarding the results, the IC_{50} values for the compounds were as follows: PFD14/A/I (N.D.μM), PFD14/B/I (60.53μM), PFD43/I (57.63μM), PFD17 (18.49μM), PFD10/A/I (46.13μM), PFD10/I/I (N.D.μM), and CBD (5.08μM). Some of the molecules could effectively protect the H9c2 cells against the H_2O_2, doxorubicin, or the simulated hypoxia/reoxygenation. CBD, used as a reference molecule, exhibited the most potent direct antioxidant effect. The western blot results show that the protective effect is potentially not coming from the endogenous antioxidant system. Taken together, the tested compounds exhibit cytoprotective effect and considerable antioxidant potential. However, further research is required particularly regarding cell survival pathways (AKT/pAKT).

Acknowledgement: *The scientific work and results published in this poster were achieved with the sponsorship of Gedeon Richter Talentum Foundation in framework of Gedeon Richter Excellence PhD Scholarship of Gedeon Richter. Supported by the University of Debrecen Program for Scientific Publication. Dr. Richárd Kajtár was supported by the PhD Excellence Scholarship from the Count István Tisza Foundation for the University of Debrecen. NKFI-143360 - Investigation of the effect of biologically active molecules in the cardiovascular system.*

OL15

Aqueous metal-free synthesis and late-stage diversification of aminated isoquinolines

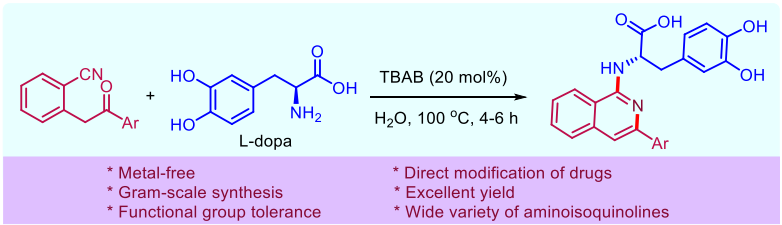
Himanshi Sharma,[a,b] Brijesh Rathi[a,b]

[a]*Laboratory for Translational Chemistry & Drug Discovery, Department of Chemistry, Hansraj College, University of Delhi, Delhi- 110007, India*
[b]*HG Khorana Centre for Chemical Biology, Department of Chemistry, Hansraj College, University of Delhi, Delhi- 110007, India*

E-mail: brijeshrathi@hrc.du.ac.in

Isoquinoline scaffolds are privileged motifs in many bioactive molecules, yet their synthesis often relies on metal catalysts, harsh reaction conditions, or organic solvents that limit late-stage functionalization of complex substrates. The presented study introduces a unified metal-free approach to the development of diversified aminated isoquinoline frameworks from 2-(2-oxo-2-aryl/alkylethyl)benzonitriles in aqueous solutions. Initially, a metal and additive free method is implemented to activate the nitrile functionality to facilitate nucleophilic addition and subsequent annulation in water. Under these mild aqueous conditions, a wide range of differently substituted primary, secondary amines and anilines undergo highly regioselective cyclization with excellent functional group tolerance and facile scalability to gram scale.

To further extend this study, direct diversification of amino acid and related drug scaffolds react smoothly with 2-(2-oxo-2-aryl/alkylethyl)benzonitriles in aqueous medium to furnish novel amino acid-substituted isoquinoline derivative. This approach tolerates multiple polar and drug-like functionalities without the need for protecting groups, providing a simple way to prepare structurally diverse isoquinoline conjugates directly from clinically relevant molecules, with gram-scale applicability. These studies collectively emphasize a metal-free, water-compatible, and versatile approach that facilitates the late-stage modification of pharmaceutically relevant amines and amino acid-based drugs, highlighting their potential for rapid library generation and further exploration in medicinal chemistry.



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OL16

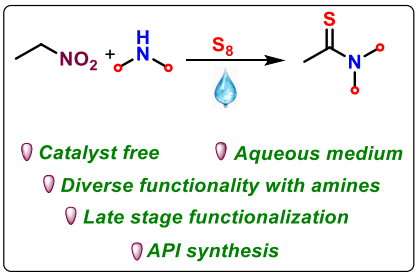
Divergent synthesis of thioamides via *umpolung* C-N bond formation

Padam Raj Bhatt,[a,b] Ankush Gupta,[a,b] Brijesh Rathi[a,b]

[a]*Laboratory For Translational Chemistry & Drug Discovery, Department of Chemistry, Hansraj College, University of Delhi, Delhi- 110007, India*
[b]*HG Khorana Centre For Chemical Biology, Department of Chemistry, Hansraj College, University of Delhi, Delhi- 110007, India*

E-mail: brijeshrathi@hrc.du.ac.in

Herein, we describe a practical water-compatible method for thioamide preparation using elemental sulfur and amines as umpolung C-N bond formation into nitroethane. The protocol is performed in aqueous media and at room temperature without recourse to harsh activators, using inexpensive elemental sulfur and nitroethane as a masked electrophilic carbon source to aid workup. The mild conditions are tolerant of a wide variety of functional groups, resulting in high yields for both primary and secondary amines and allowing for the late-stage thioamidation of drug-like molecules and API-relevant intermediates. Mechanistic studies support the formation of an electrophilic α-nitroalkyl intermediate, which reacts with amines, incorporates sulfur, and is reduced to the thioamide. This operationally simple, scalable approach provides a safer alternative for thioamide installation in medicinal chemistry.



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OL17

Repurposing SGLT2 inhibitors to mitigate doxorubicin-induced cardiac injury: focus on Dapagliflozin and Empagliflozin

Alexandra Gyongyosi,[a] Mohammadamin Biglarikhoshmaram,[a,b] Richard Kajtar,[a,b] Simon Eskeif,[a,b] Istvan Bak,[a] Istvan Lekli[a]

[a]*Department of Pharmacodynamics, Faculty of Pharmacy, University of Debrecen, H-4032, Debrecen, Hungary*
[b]*Doctoral School of Pharmacy, Medical Science Doctoral Council, University of Debrecen, H-4032, Debrecen, Hungary*

E-mail: biglarikhoshmaram@mailbox.unideb.hu

Doxorubicin (DOX) is an effective anthracycline anticancer agent, but its dose-dependent cardiotoxicity severely limits its clinical use and compromises patient outcomes. Sodium–glucose cotransporter 2 (SGLT2) inhibitors such as Dapagliflozin (DAPA) and Empagliflozin (EMPA) have demonstrated notable cardiovascular benefits, including reduced heart failure risk and cardiovascular mortality. Although multiple mechanisms contribute to DOX-induced cardiomyopathy, the molecular pathways through which DAPA and EMPA exert cardioprotective effects remain largely unresolved.

The aim of this study was to investigate the cardioprotective effects of DAPA and EMPA in a model of DOX-induced cardiotoxicity. Sprague–Dawley rats were randomly divided into four experimental groups. Animals in the DOX group received intraperitoneal injections of DOX at a dose of 2.5 mg/kg, administered six times. Rats in the DAPA- or EMPA-treated groups were given DAPA (10 mg/kg/day) or EMPA (25 mg/kg/day), respectively, by oral gavage prior to and throughout the DOX administration period. At the end of the treatment protocol, electrocardiographic (ECG) recordings were obtained, after which the hearts were isolated for ex vivo assessment of cardiac function. Histological evaluation was performed on cardiac tissue sections using hematoxylin–eosin (H&E) staining to assess general morphology and Masson's trichrome staining to determine the extent of fibrosis. Lipid peroxidation was quantified by measuring cardiac malondialdehyde (MDA) levels. Western blot analyses were conducted to examine key molecular pathways: autophagy-related proteins including p-AMPK/total AMPK, Beclin-1, LC3B, and p62; the FEM1B–FNIP1 axis; and ferroptosis-associated markers, including SLC7A11 and GPX4. Additionally, apoptosis was evaluated in cardiac sections using the TUNEL assay to determine DNA fragmentation. Together, these methodologies were employed to elucidate the mechanisms underlying the potential cardioprotective actions of DAPA and EMPA in the setting of DOX-induced cardiac injury.

Pretreatment with both DAPA and EMPA markedly ameliorated doxorubicin-induced cardiac injury. Several key parameters of cardiac function showed significant improvement compared with the DOX group, and histological analyses revealed reduced structural damage and fibrosis. In addition, DAPA and EMPA substantially decreased the extent of lipid peroxidation, as reflected by lower MDA levels, and significantly reduced the number of TUNEL-positive apoptotic cells. The SGLT2 inhibitors also modulated the autophagic pathway, as demonstrated by alterations in the expression of autophagy-related proteins. Moreover, our findings indicate that DAPA attenuated DOX-induced ferroptosis, supported by changes in ferroptosis-associated biomarkers. Nevertheless, further studies are required to clarify the mechanisms underlying the observed group-specific differences.

Acknowledgement: *This work was supported by grants NKFI-143360 and TKP2021-EGA-18, and by the University of Debrecen Program for Scientific Publication.*

OL18

EV-34, a novel H_2S-releasing ibuprofen derivative, protects against doxorubicin-induced cardiotoxicity via PI3K/AKT/FoxO3a and AMPK signaling

Simon Eskeif,[a,c] Alexandra Gyöngyösi,[a,c] Dr. Ambrus Lídia Kardosné,[a,c] Ferenc Fenyvesi,[b,c] Pál Herczegh,[d,e] Anikó Borbás,[d] Ilona Bereczki,[d,e] István Lekli,[a,c]

[a]*University of Debrecen, Faculty of Pharmacy, Department of Pharmacology, Rex Ferenc utca 1, Debrecen 4002, Hungary*
[b]*University of Debrecen, Faculty of Pharmacy, Department of Molecular and Nanopharmaceutical, Rex Ferenc utca 1, Debrecen 4002, Hungary*
[c]*University of Debrecen, Doctoral School of Pharmaceutical Sciences, Egyetem tér 1, Debrecen 4032, Hungary*
[d]*University of Debrecen, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Egyetem tér 1, Debrecen 4032, Hungary*
[e]*HUN-REN-UD Pharmamodul Research Group, University of Debrecen, Egyetem tér 1, Debrecen 4032, Hungary*

E-mail: eskeif.simon@mailbox.unideb.hu

Doxorubicin remains one of the most effective chemotherapeutic agents for the treatment of both solid and hematological malignancies; however, its clinical application is significantly restricted by cumulative cardiotoxicity. Although the mechanisms underlying DOX-induced cardiac injury are multifactorial and incompletely understood, increasing evidence suggests that impaired endogenous hydrogen sulfide (H_2S) production contributes substantially to cardiomyocyte damage. In this study, we investigated the cardioprotective potential of EV-34, a newly developed H_2S-releasing ibuprofen derivative synthesized according to the method described by Gyöngyösi et al. EV-34 significantly alleviated DOX-induced cardiac injury by attenuating oxidative stress, mitochondrial dysfunction, and apoptotic signaling. Furthermore, EV-34 increased intracellular H_2S levels both in the presence and absence of DOX, likely through combined direct H_2S release and stimulation of endogenous H_2S biosynthesis pathways. Mechanistically, EV-34 reduced intracellular reactive oxygen species (ROS) formation, suppressed mitochondrial superoxide accumulation, and enhanced mitochondrial superoxide dismutase expression. In parallel, EV-34 activated the PI3K/AKT/FoxO3a and AMPK signaling pathways while inhibiting apoptosis through downregulation of caspase-3 activation. The effects of EV-34 were compared with those of the established slow-releasing H_2S donor GYY4137. Collectively, these findings highlight EV-34 as a promising therapeutic candidate for the prevention and treatment of DOX-induced cardiotoxicity.

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OL19

Steady-state concentrations of clarithromycin under different routes of administration in pneumonia: risk-factors and clinical outcomes

Adina Fésüs,[a] Éva Kovács,[a] Zsanett Szilágyi,[a,b] István Bak,[a] Ildikó Bácskay,[c] István Lekli,[a] Attila Vaskó[d]

[a]*Department of Pharmacodynamics, Faculty of Pharmacy, University of Debrecen, H-4032, Debrecen, Hungary*
[b]*Doctoral School of Medical Sciences, University of Debrecen, H-4032, Debrecen, Hungary*
[c]*Department of Pharmaceutical Technology, Faculty of Pharmacy, University of Debrecen, H-4032, Debrecen, Hungary*
[d]*Department of Pulmonology, Faculty of Medicine, University of Debrecen, H-4032, Debrecen, Hungary*

E-mail: *szilagyi.zsanett@pharm.unideb.hu*

Background: Appropriate antibiotic dosage is crucial for improving outcomes in critically ill patients facing pneumonia.

Aims and objectives: Our research aimed to evaluate the development of the steady-state concentration (Css) of clarithromycin (CLAR) in this specific patient population with different routes of administration, to identify the influencing factors, and to examine the relationship between clinical outcomes and Css.

Materials and methods: This study was conducted as a single-center prospective observational study in the ICU of a pulmonology department between 2 February 2025 and 05 December 2025. The study target group included all adult patients (n=72) treated primarily with empirical CLAR (500 mg two times a day, n=70 cases; corrected to kidney function, n=2 cases) due to pneumonia. Blood sample collection was performed on day 3 of the CLAR administration, when 5 samples were taken as follows: at steady-state before drug administration and 1, 2, and 3 hours after intravenous (IV), oral (PO), and nasogastric (NG) drug administration, while one sample for albumin level. Determination of CLAR serum concentrations was determined by LC-MS/MS using a CLAR European Pharmacopeia Reference Standard by Merck. The study received ethics approval (DE RKEB/IKEB: 7094-2025).

Results: CLAR serum levels followed the expected pharmacokinetics for all three routes of administration. The CLAR Css was 3-fold higher for PO (n=30) than for IV (n=27) administration and 2.7-fold higher for NG (n=15) administration (6.13 vs 2.05 μg/ml and 6.13 vs 2.26 μg/ml, $p<0.05$). Severe reduction of CrCl (<59ml/min) increased serum levels for all administration routes. CLAR serum levels increased proportionally with increasing albumin serum levels (as the faster clearance of the free fraction resulted in lower serum levels, especially for IV) and with the increasing CCI (Charles Comorbidity Index). No significant difference in length of stay (LOS) and in survival was found between IV and PO administration (81 and 83%), however, the probability of survival was significantly lower (40%) in the case of NG administration.

Conclusions: PO administration presented the highest CLAR Css levels. CrCl, albumin levels, and CCI were found to be influencing factors of CLAR Css. PO and IV administration resulted in similar clinical outcomes; however, the lower survival rate associated with higher Css values in case of NG administration requires further investigation.

OL20

Synthesis and investigation of α-santonin derivatives linked to N-, S- and O-heterocycles *via* a 1,2,3-triazole linker

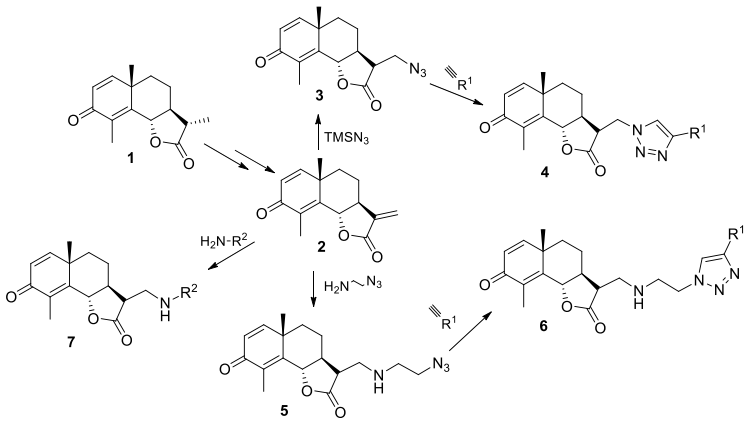
Mária Fanni Boncz,[a] Eszter Kónya,[a] Kitti Tari,[b] András Szekeres,[b] Adriána Kovács,[c] István Zupkó,[c] Le Minh Tam,[a,d] Zsolt Szakonyi[a]

[a]*Institute of Pharmaceutical Chemistry, University of Szeged, Eötvös utca 6, H-6720 Szeged, Hungary*
[b]*Department of Biotechnology and Microbiology, University of Szeged, Közép fasor 52, H-6726 Szeged, Hungary*
[c]*Institute of Pharmacodynamics and Biopharmacy, University of Szeged, Eötvös utca 6, H-6720 Szeged, Hungary*
[d] *HUN-REN-SZTE Stereochemistry Research Group, University of Szeged, Eötvös u. 6, H-6720 Szeged, Hungary*

E-mail: bonczmaria@gmail.com

α-Santonin, a sesquiterpene lactone, have been reported as anticancer, antifungal, antipyretic, and anti-inflammatory agents. Interestingly, many *α*-santonin derivatives presented more and better bioactivities, such as anti-cancer, herbicidal immunosuppressant, phytotoxic, anti-angiogenic [1].

A new series of α-santonin derived 1,4-disubstituted-1,2,3-triazoles conjugates were synthesised and evaluated for their *in vitro* antiproliferative and antimicrobial effects. The key intermediate, 11-*exo*-methylene-santonin (**2**), prepared from commercially available *α*-santonin (**1**) in two steps according to literature procedure [2], was subjected to Michael addition with $TMSN_3$ [3] or aminoethylazide [4] to produce the corresponding azides (**3**) and (**5**), respectively. Subsequently, all these azides used in regioselective Huisgen 1,3-dipolar cycloaddition reactions (Click chemistry) with diverse heterocyclic alkynes to afford different 1,2,3-triazole derivatives (**4**) and (**6**) [3]. On the other hand, nucleophilic addition between (**2**) and various heterocyclic amine was successfully performed to furnish the target *β*-aminolactones (**7**) [2]. The antiproliferative and antimicrobial activity of all santonin derivatives is under investigated in a collaborative effort with respect to significant effects.



Scheme 1: Preparation of santonin derivatives

Acknowledgement: *I am grateful to the EKÖP for its support (EKÖP-191-SZTE).*

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OL21

In vitro antiproliferative effects of novel 5-fluorouracil derivatives on HeLa cell line

Bálint Lakó[a]

[a]*Institute of Pharmacodynamics and Biopharmacy, Faculty of Pharmacy, University of Szeged, 6720 Szeged, Eötvös u. 6., Hungary*

E-mail: lakbalal25@gmail.com

Of the 24 Biginelli hybrids, which are analogs of 5-fluorouracil (5-FU), and were previously investigated, two compounds exhibited outstanding antiproliferative activity against HeLa cells, surpassing the efficacy of 5-FU. Both compounds exhibited tumor-selective activity when tested on intact mouse fibroblasts [1].
Our goal is to characterize the anticancer mechanisms of action of these two potent Biginelli hybrids on HeLa cells.

We examined the compounds' effects on cell morphology and membrane damage by measuring LDH activity and using fluorescent double staining; we analyzed cell cycle changes by flow cytometry; and we extended the assessment of tumor selectivity to the intact, human h-TERT HME1 cell line.
Compared to cisplatin, our compounds initiated a lesser increase in LDH activity. However, they induced DNA condensation and degradation, which are characteristic of apoptosis, in HeLa cells. Flow cytometry measurements confirmed the formation of a subG1 population and revealed a significant increase in the proportion of cells in the G1 phase. The NJ-617 derivative inhibited the division of intact human cells only at significantly higher concentrations.

The tested Biginelli hybrids do not directly damage cell membrane; however, they induce apoptosis and cause cell cycle arrest in the G1 phase. The tumor selectivity of the NJ-617 derivative can also be demonstrated in intact human cells. The Biginelli derivatives may represent a promising alternative in the drug therapy of cervical cancer and could serve as a good starting point for the development of new, tumor-selective active compounds.

Acknowledgement: *TKP-2021-EGA-32 and OTKA 143690*

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OL22

Antioxidant and anti-inflammatory effects of newly synthesized CBG/CBD derivatives

Boglárka Polónyi[a]

[a]*Department of Pharmacodynamics, Faculty of Pharmacy, University of Debrecen, H-4032, Debrecen, Hungary*

E-mail: boglarka.polonyi@gmail.com

Introduction: *Cannabis sativa* is one of the longest-studied medicinal plants on Earth. While the most well-known cannabinoid is -THC, we are aware of far more components with therapeutic effects. Our research focuses on two major cannabinoids: cannabidiol (CBD) and cannabigerol (CBG). An increasing number of beneficial properties are attributed to these two compounds, including anti-inflammatory, neuroprotective, and antioxidant effects. Bixin, a bioactive component of *Bixa orellana*, is also known to be capable of reducing the expression of certain anti-inflammatory factors. However, it is true for both types of phytochemical compounds that their pharmacological application is limited due to their chemical and physical properties; specifically, they are characterized by poor water solubility and, in some cases, instability. A potential solution to this issue could be the newly synthesized CBD and CBG derivatives created by coupling them with bixin, which are the focus of our work.

Objectives: Since we were able to demonstrate antioxidant effects based on our previous investigations, we ultimately took two directions when designing further experiments : we were curious about the potential protective effects of the compounds in myocardial injury, as well as the extent of their anti-inflammatory effects, following the results of previous studies.

Materials and Methods: Their antioxidant properties were investigated on cardiomyocytes (H9c2), in which myocardial injury was modeled using hypoxic conditions. The changes in the levels of various antioxidant proteins (catalase, SOD, HO-1) were analyzed via Western blot. Furthermore, the expression of genes involved in inflammatory signaling (including *IL-1B*, *IL-10*) was examined using RT-qPCR on MCF-7 cells in inflammation artificially induced by TNF-alpha.

Results and Discussion: Based on the results of our Western blot analysis, the new cannabinoid derivatives increased the levels of endogenous antioxidant enzymes, thereby providing a protective effect against oxidative stress and hypoxic conditions. Additionally, from our PCR investigations, we observed changes in the genes involved in inflammation. Proving the beneficial effects of these favorably modified cannabinoids could lead to completely new therapeutic developments; therefore, we consider their investigation to be of extraordinary importance.

OL23

Neuraminidase inhibitor-based hydrophobic tags

Miklós Lovas,[a,b] Miklós Bege,[a,c] Anikó Borbás[a]

[a]*University of Debrecen, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, 4032, Debrecen, Hungary*
[b]*Doctoral School of Medical Sciences, University of Debrecen, 4032, Debrecen, Hungary*
[c]*National Laboratory of Virology, Szentágothai Research Centre, University of Pécs, 7624, Pécs, Hungary*

E-mail: lovas.miklos@pharm.unideb.hu

Neuraminidase inhibitors (NIs) are the most prominent antivirals available against influenza infections: by occupying the binding pocket of influenza neuraminidase, they inhibit the release of viral particles from infected cells, slowing the spread of the virus between cells. Due to the genetic drift and shift of influenza viruses, resistance against NIs can develop spontaneously, necessitating the need for the development of novel antivirals and the improvement of currently available drugs [1]. The purpose of our work is the development of targeted influenza neuraminidase degraders based on the two globally approved NIs zanamivir and oseltamivir.

Targeted protein degradation is an exciting approach in drug design which hijacks the cell machinery to induce the proteolysis of proteins of interest (POIs). About a dozen different modalities are known by now, some with clinical validation (e.g. the PROTAC vepdegestrant, or the molecular glue pomalidomide), and with each coming with its own scope and limitations [2]. A less commonly used, but very promising approach is hydrophobic tagging (HyTag), which mimics the misfolding or denaturation of POIs to induce their degradation. By connecting a POI ligand with a compact hydrophobic group, such as adamantane, the hydrophobic surface area of the POI is increased, which the cell recognizes as damage, setting the protein up for degradation. This approach is especially well suited for polar ligands (such as the extremely polar zanamivir), unlike the more popular PROTAC approach, which generally requires POI ligands of lower polarity for efficacy [3].

The focus of this work is the modular synthesis of NI-adamantane-conjugates, with the two parts being connected in two different positions by linkers of various sizes and rigidity, in order to generate a molecular library for later biological studies (Figure 1).

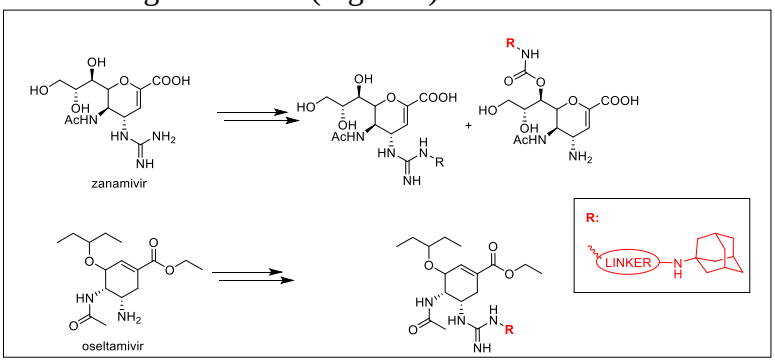

Figure 1. Synthesis of zanamivir- and oseltamivir-based Hy-tags targeting influenza neuraminidase

Acknowledgement: *Supported by the EKÖP-25-2-DE-116 University Research Scholarship Program of the Ministry for Culture and Innovation from the source of the National Research, Development and Innovation Fund. This research work was conducted with the support of the National Academy of Scientist Education Program of the National Biomedical Foundation under the sponsorship of the Hungarian Ministry of Culture and Innovation.*

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OL24

Harnessing oxa-Pictet-Spengler, Pictet-Spengler, and thiol-ene coupling reactions to construct thioglycoside-heterocycle conjugates as *Pseudomonas aeruginosa* LecA and LecB inhibitors

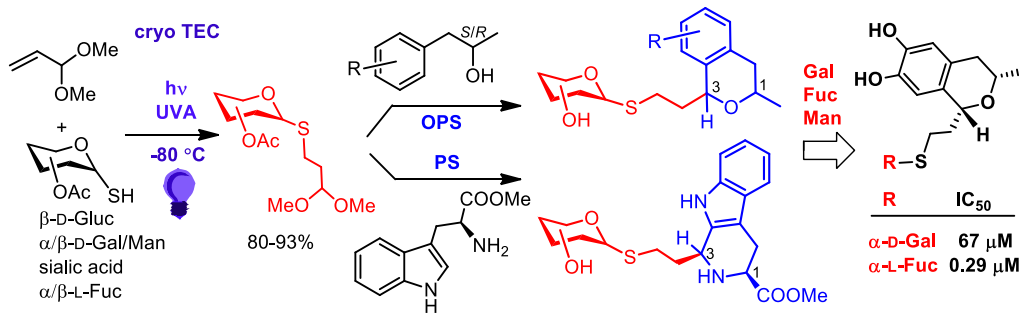
Nawar Ahmad,[a,b] Ágnes Homolya,[a] Beshoy Tawfik,[c] Alexander Titz,[c] Anikó Borbás[a]

[a]*Department of Pharmaceutical Chemistry, University of Debrecen, Egyetem tér 1, H-4032, Debrecen, Hungary*
[b]*Doctoral School of Pharmaceutical Sciences, University of Debrecen, H-4032, Debrecen, Hungary*
[c]*Chemical Biology of Carbohydrates (CBCH), Helmholtz-Institute for Pharmaceutical Research Saarland*

Email: nawar.ahmad@pharm.unideb.hu, borbas.aniko@pharm.unideb.hu

The development of stable carbohydrate mimetics capable of targeting carbohydrate-binding proteins remains an attractive strategy for the discovery of novel anti-infective and therapeutic agents. Among these, thioglycosides, as hydrolysis-resistant analogues of natural *O*-glycosides, offer enhanced metabolic stability while preserving the key lectin-recognition features [1, 2]. Expanding their structural diversity through conjugation with biologically relevant heterocycles, such as isochroman and tryptoline motifs, may provide access to compounds with improved recognition properties and biological activity. However, the potential of glycomimetics containing isochroman and tryptoline aromatic aglycones in lectin inhibition has not yet been explored.

Herein, we present a synthetic platform for the construction of isochroman- and tryptoline-based thioglycoside conjugates, employing glycosylthiols, phenethyl alcohol/tryptophan, and acrolein dimethyl acetal building blocks, by integrating oxa-Pictet–Spengler/Pictet–Spengler cyclization reactions with the low-temperature photoinitiated thiol–ene coupling (cryo TEC) reaction [3]. Sequential inversion of the cyclization and thiol–ene steps enabled stereoselective access to structurally diverse heterocycle-conjugated thioglycosides.



The biological relevance of the synthesized ligands was investigated through their interaction with the virulence-associated LecA and LecB lectins of *Pseudomonas aeruginosa*, using competitive fluorescence polarization assays [4]. These compounds displayed remarkable lectin inhibition, with clear dependence on both carbohydrate identity and the aromatic aglycone substitution, highlighting structure-dependent recognition effects.

Acknowledgment: *This research was supported by the University of Debrecen Program for Scientific Publication.*

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OL25

New class of uridine- and adenosine-based morpholino-nucleosides as potential anti-SARS-CoV-2 agents

Rasha Ghanem Kattoub,[a,b] Miklós Bege,[a] Erika Hevesi-Mező,[a] Anikó Borbás[a]

[a]*Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Debrecen, 4032, Debrecen, Hungary*
[b]*Doctoral School of Pharmaceutical Sciences, University of Debrecen, 4032, Debrecen, Hungary*

E-mail: rasha.ghanemkattoub@pharm.unideb.hu

Over the past few decades, nucleoside analogs have been at the forefront of the search for novel therapeutic agents. One significant class of these analogs is morpholino-nucleosides, which have seen huge success in antisense-based treatment, with 4 FDA-approved drugs [1]. Nevertheless, much less effort has been employed to explore the potential biological activities of substituted morpholino-nucleoside monomers. On the other hand, conformational restriction has been proven to be a highly effective method for enhancing the binding affinity of nucleos(t)ides to a specific target, thereby increasing biological activity [2]. However, synthesizing such analogs is challenging due to the complex, multi-step synthesis and the need for precise control over regio- and stereochemistry. Herein, we present a novel reductive aminocyclization strategy that utilizes bifunctional amines with nucleoside secodialdehydes. This approach enables the single-step synthesis of a novel fused bicyclic, as well as a new type of *N*-substituted monocyclic morpholino-nucleosides (**Figure 1**).

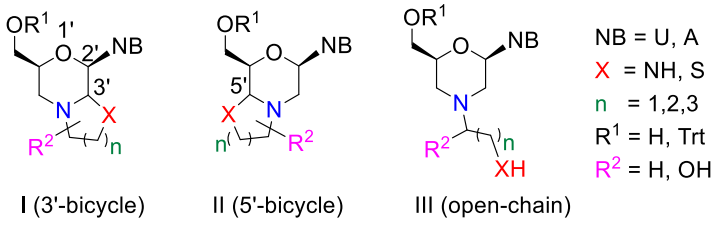

Figure 1: General Structure of novel morpholino-nucleosides

As a result of our thorough optimization of the reaction conditions, two major routes were proven to be effective - the $ZnCl_2$-mediated method and the glacial acetic acid strategy - affording a diverse range of 3′- and 5′-bicyclic morpholino-uridine and adenosine (**General structures I and II**, respectively), as well as open-chain products (**General structure III**). A total of 44 novel morpholino derivatives were synthesized and subsequently evaluated for their anti–SARS-CoV-2 activity. Among these, six bicyclic derivatives exhibited significant antiviral effects, with three compounds belonging to general structure **I** identified as the most potent. To elucidate their mode of action, multiple stages of the SARS-CoV-2 replication cycle were examined. The results indicate that all tested compounds act at the later stages of viral replication. Furthermore, molecular docking studies of these analogs with SARS-CoV-2 target proteins were performed, providing additional insight into their potential mechanisms of action.

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OL26

Synthesis and galectin inhibitory activity of new β-D-galactopyranosyl azoles

István Kacsir,[a] Sándor Kun,[a] Ágnes Homolya,[a] Levente Homolya,[a] Samreen Saifi,[a,b] Tímea Kaszás,[a] Mariann Kiss,[a] Aliz Rimóczi,[a] László Juhász,[a] Éva Juhász-Tóth,[a] Marietta Tóth,[a] Ulf J. Nilsson,[c] László Somsák,[a] Éva Bokor[a]

[a] *Department of Organic Chemistry, University of Debrecen, P.O. Box 400, H-4002, Debrecen, Hungary*
[b] *Doctoral School of Chemistry, University of Debrecen, P.O. Box 400, H-4002, Debrecen, Hungary*
[c] *Department of Chemistry, Lund University, P.O. Box 124, SE-22100, Lund, Sweden*

E-mail: kacsir.istvan@science.unideb.hu, bokor.eva@science.unideb.hu

Galectins are carbohydrate-recognizing proteins (lectins) with binding preference for molecules containing β-galactoside scaffold. They play important roles in various intra- and extracellular regulatory processes such as cell adhesion, migration, proliferation, host defence, survival and cell death. Thus, galectins and compounds capable of influencing their activity have a high therapeutic potential e.g. in cancer, fibrosis, inflammation, Alzheimer's and autoimmune diseases [1]. Many synthetic sugar-based inhibitors are known [1], among them a β,β-thiodigalactoside (TD139) [2] and an α-thiogalactoside (GB1211) [3] have reached clinical trials for the treatment of idiopathic pulmonary fibrosis and cancer, respectively. Recently, five-membered β-D-galactopyranosyl heterocycles (1,2,3-triazoles, oxazoles, izoxazoles and pyrazoles) have appeared as a new inhibitor class [4]. Based on their inhibitory potency against galectin-1 and galectin-3 it can be assumed that the heterocycle has a decisive effect on the selectivity. 1,2,3-Triazoles show a higher affinity to galectin-1, oxazoles prefer galectin-3, while pyrazoles and isoxazoles display negligible selectivity [4]. To get a deeper insight into the structure-activity relationships of this inhibitor family we aimed to extend the above series with the constitutional isomers of 1,2,3-triazoles and isoxazoles and further β-D-galactopyranosyl azoles, such as thiazoles, imidazoles, 1,3,4- and 1,2,4-oxadiazoles, 1,2,4-triazoles and tetrazoles. In the presentation the syntheses of the new galactosyl heterocycles and their biological results will be reported.

Acknowledgement: *The research was supported by the National Research, Development and Innovation Office of Hungary (K146147, PD142641, 2024-1.2.3-HU-RIZONT-2024-00005).*

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OL27

Photoinitiated thiol-ene reactions of glycals for the synthesis of galectin inhibitors

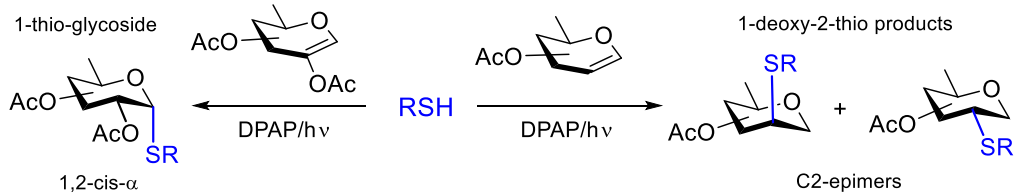
Ágnes Homolya,[a] Nawar Ahmad,[a,b] Rasha Ghanem Kattoub,[a,b] Fanni Hőgye,[a] Erika Mező,[a] Ulf J. Nilsson,[c] Anikó Borbás[a]

[a]*Department of Pharmaceutical Chemistry, University of Debrecen, H-4032, Debrecen, Hungary*
[b]*Doctoral School of Pharmaceutical Sciences, University of Debrecen, H-4032, Debrecen, Hungary*
[c]*Department of Chemistry, Lund University, S-22100, Lund, Sweden*

E-mail: homolya.agnes@pharm.unideb.hu

Thioglycosides and sulfur-containing glycomimetics exhibit high stability under physiological conditions due to their resistance to acidic and enzymatic hydrolysis, which makes them attractive structures for the development of carbohydrate-based drug candidates [1]. Thioglycosides and sulfur-linked glycomimetics can be synthesized via the photoinitiated thiol-ene reaction, which serves as a metal-free click chemistry approach [2].

In this lecture a comparative study on the thiol-ene reactions of C2-substituted and unsubstituted glycal derivatives with some selected thiols (thioacetic acid, tert-butyl mercaptan, thiosugar derivatives) will be presented. The yields, regio- and stereoselectivity were studied depending on the thiol and temperature. 2-Acetoxyglycals gave the 1,2-*cis*-α products with complete regio- and stereoselectivity, while unsubstituted glycals gave the 1-deoxy-2-thiolated compounds regioselectively, in most cases as C2-epimers [3].



Scheme 1: Regio- and stereoselectivity of the thiol-ene coupling reaction

The synthetized compounds were tested as Gal-1, Gal-3 and Gal-8N inhibitors, and some of the compounds showed better inhibition than a high affinity β,β-thiodigalactoside.

Acknowledgement: *The research was supported by the National Research, Development and Innovation Office of Hungary OTKA PD 146805 and by the University of Debrecen Program for Scientific Publication.*

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OL28

i-Motif studies: synthetic and biochemical

Lajos Kovács,[a] Zoltán Kupihár,[a] Györgyi Ferenc,[b] Péter Burkovics,[b] Dzsenifer Török[b]

[a]*University of Szeged, H-6720, Szeged, Hungary*
[b]*Biological Research Center, H-6726, Szeged, Hungary*

E-mail: kovacs.lajos@med.u-szeged.hu

Nucleic acids form highly polymorphic structures. Beyond the well-known canonical double helix, alternative conformations featuring triplexes, G-quadruplexes, pentaplexes, stem loops, pseudoknots, and Holliday junctions are also possible, as are i-motifs. While the formation of G4 structures in living cells is widely accepted, the presence and formation of i-motifs (intercalated motifs, IMs) is still debated [1].

An i-motif is a four-stranded quadruplex nucleic acid structure formed by two parallel duplexes arranged antiparallel by intercalating hemiprotonated $^{+}$C-H···C base pairs. IMs are most stable *in vitro* at low temperatures and acidic pH levels (around pH 4.5), though some IM structures are also stable at neutral pH [2]. Therefore, it has long been considered that this structure cannot form *in vivo*. However, there is growing evidence that IMs are present in vivo and play a crucial role in regulating gene expression. Since all complementary strands of G4-prone sequences can form IMs, they could play an important role in regulating the expression levels of oncogenes. However, the inherent lability of IM structures makes studying them difficult. Several approaches aim to overcome this hurdle, such as 2'-deoxypseudoisocytidine, FANA ONs, and metal-ion-mediated IMs. Herein, we propose 6-oxocytidine derivatives that possess a tautomeric form suitable for IM formation, independent of the environment's pH. The lecture also outlines our results on IM-binding protein WRNIP1 [3].

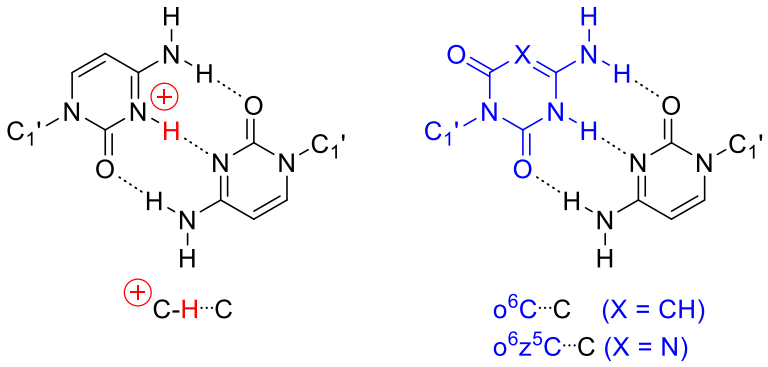

Figure 1: i-Motif's main structural element (left) and 6-oxocytidine analogues (right)

Acknowledgement: *This work was supported by the SZAOK-SZBK Collaboration Research Grant of the Albert Szent-Györgyi Medical School, University of Szeged, Hungary.*

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OL29

Synthesis of novel alkylthioether-alpha-cyclodextrin derivatives and their impact on bacterial biofilm formation

István Kese,[a,b] Levente Szőcs,[b,c] Róbert Iványi,[b] Éva Fenyvesi,[b] Mónika Molnár,[a]

[a]Department of Applied Biotechnology and Food Science, Budapest University of Technology and Economics, Szt. Gellért tér 4., Budapest, 1111, Hungary
[b]CycloLab Cyclodextrin Research and Development Laboratory Ltd., Illatos út 7., Budapest, 1097, Hungary
[c]Department of Pharmaceutical Chemistry, Semmelweis University, H-1092 Hőgyes E. u. 9., Budapest, Hungary

E-mail: keseistvan@edu.bme.hu, istvan.kese@cyclolab.hu,

Bacterial communication, called *Quorum Sensing* (QS) is a cell density dependent signaling process that allows the microbial population to behave as a multicellular organism in colonizing the host, forming biofilms, producing virulence factors, and thus adapting to changing environments. This communication system is based on the production and detection of extracellular signal molecules (called autoinducers), e.g. acyl-homoserine lactone type signals, (AHLs) [1]. The inhibition of QS, *Quorum Quenching* (QQ) involves several different molecules and methods, which have in common, that they do not kill or exert selective pressure on the bacteria, as the conventional antibiotics do, but only prevent communication between cells. Direct modulation of this microbial communication is a new wave strategy avoiding microbial resistance; a potential tool for inhibiting QS is trapping the signal molecules [2].

Nowadays, cyclodextrins (CDs) are widely used due to their ring structure and their ability to form inclusion complexes. According to previous studies, they can reversibly encapsulate the AHL molecules in Gram-negative bacteria, preventing them from binding to the receptors and interrupting the communication [3,4].

The aim of the research was to develop a series of water-soluble mono-alkylthioether-αCD derivatives randomly substituted with sulfobutyl (SB), hydroxypropyl (HP), quaternary amino (QA) functional groups with high complexation rate to signal molecules and a novel synthetic approach. These derivatives were characterized using NMR techniques, HPLC-MS and CE. Furthermore, short-term microbiological study was performed with the synthetized water-soluble alkylthioether-αCD derivatives to systematically investigate the potential QS-disrupting ability and compare their effect on the biofilm formation of *Pseudomonas aeruginosa*. According to the results the contact time, the temperature and also the structure of the derivatives (length of alkyl chain, type of the substituent to improve the solubility) had a significant influence on both the viability of the cells and on the biofilm formation.

Acknowledgement: *Project No. 2024-2.1.2-EKÖP-KDP-2024-00005 and TKP2021-EGA-02 has been implemented with the support provided by the Ministry of Culture and Innovation of Hungary from the National Research, Development and Innovation Fund, financed under the EKÖP_KDP-24-1-BME-36 and the TKP2021-EGA funding scheme.*

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OL30

β-Cyclodextrin dimers: complexation and enantiomer recognition of chiral cationic and anionic APIs using capillary electrophoresis

Zsolt Ürögi,[a,b] Róbert Iványi,[c] Dominika Mária Herr,[b,d] István Kese[a,e], Erika Bálint,[a], Béla Mátravölgyi[a]

[a]*Department of Organic Chemistry and Technology, Faculty of Chemical Technology and Biotechnology, Budapest University of Technology and Economics, H-1111 Budapest, Hungary*
[b]*CycloLab Cyclodextrin Research and Development Laboratory Ltd., H-1097 Budapest, Hungary*
[c]*Bio-Sol-Dex Ltd., H-6000 Kecskemét, Hungary*
[d]*Department of Pharmaceutical Chemistry, Semmelweis University, H-1092 Budapest, Hungary*
[e]*Department of Applied Biotechnology and Food Science, Faculty of Chemical Technology and Biotechnology, Budapest University of Technology and Economics, H-1111 Budapest, Hungary*

E-mail: zsolt.urogi98@edu.bme.hu

Synthesis of several cyclodextrin dimers has been previously reported [1], however their general applicability has not been studied thoroughly. The aim of our research is to synthetize four novel single-isomer β-cyclodextrin dimers with triazole linkage [2] and study their complexation properties towards the enantiomers of chiral cationic and anionic APIs using capillary electrophoresis [3].

We theorize that the headphone like structure of the dimers (Fig. 1) can encapsulate the guest molecules on both ends which will result in a change of the complex stability constant and possibly in better enantiomer recognition due to the dual complexation. It is easy to see that the size and length of the guest molecules have a major impact on our proposed complexation mechanism. To better understand this effect, we prepared four β-cyclodextrin dimers with various chain-length linkers and compared their complexation properties against the native β-cyclodextrin.

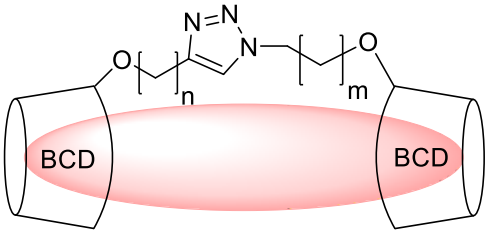

Figure 1: General structure and proposed complexation mechanism of the β-cyclodextrin dimers

Acknowledgement: *The research was supported by the NKFIH grant number FK-142712.*

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OL31

Conformation-activity relationships in synthetic heparin pentasaccharides revealed by integrative structural analysis

Viktória Goldschmidt Gőz,[a] Dávid Papp,[a,b] Mihály Herczeg,[c] Gitta Schlosser[a]

[a]*MTA-ELTE Lendület (Momentum) Ion Mobility Mass Spectrometry Research Group, ELTE Eötvös Loránd University, Pázmány Péter sétány 1/A, H-1117 Budapest, Hungary Postcode, City, Country*
[b]*Hevesy György PhD School of Chemistry, Institute of Chemistry, Eötvös Loránd University, Pázmány Péter sétány. 1/A, H-1117 Budapest, Hungary*
[c]*Department of Chemistry, Eszterházy Károly Catholic University, Leányka utca 12, H-3300 Eger, Hungary*

E-mail: viktoria.goz@ttk.elte.hu

Heparin is a widely used carbohydrate-based anticoagulant, yet the structural characterization of its synthetic analogues remains challenging due to their pronounced conformational flexibility. In particular, the L-hexuronic acid unit plays a key role in biological activity, as its conformation strongly influences function.

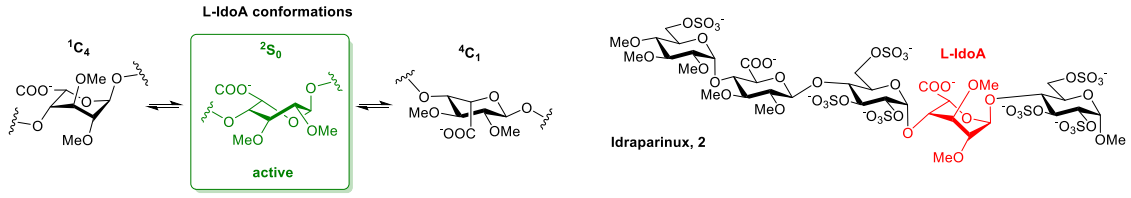

Figure 1: Structure of heparin analogue Idraparinux (2). Possible conformations of L-iduronic acid (L-IdoA) unit in showung the $^{2}S_{O}$ conformer in green, responsible for biological activity

In this study, synthetic heparin analogue pentasaccharides exhibiting a broad range of biological activities (1–112%) were investigated using an integrative structural approach combining cyclic ion mobility-mass spectrometry (cIM-MS), tandem MS (MS/MS), and previously reported biological activity and NMR data. Highly active compounds were found to adopt a single dominant conformational state, while less active analogues exhibited multiple coexisting conformers.

Fragmentation behavior was evaluated as a function of collision energy, revealing characteristic fragmentation patterns associated with different conformational families. Active compounds showed highly consistent fragmentation fingerprints, whereas low-activity and inactive analogues displayed distinct and differentiable patterns, including the presence of diagnostic fragment ions.

These results demonstrate that conformational heterogeneity directly correlates with biological activity and that fragmentation-based signatures provide a powerful tool for distinguishing conformational states. This approach offers new opportunities for understanding structure-activity relationships and supports the rational design of heparin-based therapeutics.

Acknowledgement: *This project was supported by the Lendület (Momentum) Program of the Hungarian Academy of Sciences (HAS, MTA) and by the National Research, Development and Innovation Office of Hungary (project No. SNN 148580).*

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OL32

A brief overview of the research group's work

Dénes Páll[a]

[a]*Gyógyszer- és Élelmiszerfejlesztési Koordinációs Központ, 4032, Debrecen, Hungary*

E-mail: pall.denes@unideb.hu

OL33

Therapeutic aspects of *Prunus cerasus* extract in a rabbit model of atherosclerosis-associated diastolic dysfunction

Reka Szekeres,[a] Daniel Priksz,[a] Rita Kiss,[a] Mariann Bombicz,[a] Balazs Varga,[a] Rudolf Gesztelyi,[a] Anna Szilagyi,[a] Barbara Takacs,[a] Vera Tarjanyi,[a] Beata Pelles-Tasko,[a] Ildiko Forgacs,[b] Judit Remenyik,[b] Zoltan Szilvassy,[a] Bela Juhasz[a]

[a]*Department of Pharmacology and Pharmacotherapy, Faculty of General Medicine, University of Debrecen, H-4032, Debrecen, Hungary*
[b]*Center for Complex Systems and Microbiome Innovations, Faculty of Agricultural and Food Sciences and Environmental Management, University of Debrecen, H-4032, Debrecen, Hungary*

E-mail: juhasz.bela@med.unideb.hu

This study evaluates the potential therapeutic effects of anthocyanin-rich *Prunus cerasus* (sour cherry) extract (PCE) on atherosclerosis-associated cardiac dysfunction, described by the impairment of the NO-PKG (nitric oxide–protein kinase G) pathway and the antioxidant capacity. Initially, a rabbit model of atherosclerotic cardiovascular disease was established by administering a cholesterol-rich diet, enabling the examination of the impact of 9 g/kg PCE on the pre-existing compromised cardiovascular condition. After that, the animals were divided into four groups for 12 weeks: the (1) untreated control group; (2) PCE-administered healthy rabbits; (3) hypercholesterolemic (HC) group kept on an atherogenic diet; and (4) PCE-treated HC group. Dyslipidemia, impaired endothelial function, and signs of diastolic dysfunction were evident in hypercholesterolemic rabbits, accompanied by a reduced cardiac expression of eNOS (endothelial nitric oxide synthase), PKG, and SERCA2a (sarco/endoplasmic reticulum calcium ATPase 2a). Subsequent PCE treatment improved the lipid profile and the cardiac function. Additionally, PCE administration was associated with elevated myocardial levels of eNOS, PKG, and SERCA2a, while no significant changes in the vascular status were observed. Western blot analysis further revealed hypercholesterolemia-induced increase and PCE-associated reduction in heme oxygenase-1 expression. The observed effects of anthocyanins indicate their potential as a valuable addition to the treatment regimen for atherosclerosis-associated cardiac dysfunction.

Keywords: HO-1, PKG, Prunus cerasus, SERCA2a, anthocyanins, cardiac dysfunction, eNOS

Acknowledgement: *Supported by GINOP-2.2.1-15-2017-00079, GINOP-2.3.4-15-2016-00002, TKP2020-IKA-04, TKP2021-EGA-18, TKP2020-NKA-04, and ÚNKP-22-3 projects.*

OL34

Evaluation of *Echinacea* leaf extract and allantoin based topical formulations in an imiquimod-induced psoriasis-like model

Cristina Burlou-Nagy (Fati),[a,b] Annamaria Pallag,[a,b], Laura Grațiela Vicaș,[b] Octavia Gligor, [c] Tünde Horvath,[b] Beáta Lelesz,[4] Csaba Hegedűs,[4] Imre Leiter,[4] Béla Juhász,[4] Rita Kiss[d]

[a]*Doctoral School of Biological and Biomedical Sciences, University of Oradea, 410087, Oradea, Romania*
[b]*Department of Pharmacy, Faculty of Medicine and Pharmacy, University of Oradea, 410073, Oradea, Romania*
[c]*Department of Preclinical Disciplines, Faculty of Medicine and Pharmacy, University of Oradea, 410073, Oradea, Romania*
[d]*Department of Pharmacology and Pharmacotherapy, Faculty of Medicine, University of Debrecen, H-4032, Debrecen, Hungary*

E-mail: kiss.rita@med.uneb.hu

Psoriasis is a chronic inflammatory disorder characterized by epidermal hyperproliferation and immune dysregulation. This study evaluated the topical efficacy of Echinacea leaf extract and allantoin compared to a corticosteroid (mometasone furoate) in an imiquimod (IMQ)-induced psoriasis-like model in Sprague-Dawley rats. Psoriasiform lesions were induced by daily application of 5% IMQ for six days, followed by six weeks of treatment with one of the following formulations: *Echinacea* cream or gel, allantoin cream or gel, and mometasone. Disease severity was assessed using a modified Psoriasis Area and Severity Index (PASI) and histological analysis. All groups developed psoriasis-like lesions; however, *Echinacea* cream produced the most pronounced and sustained reduction in PASI scores, with near-complete macroscopic recovery. *Echinacea* gel and allantoin cream showed moderate effects, while allantoin gel and mometasone exhibited limited efficacy. Histological findings supported these results, with *Echinacea* cream restoring near-normal epidermal architecture. In conclusion, topical *Echinacea* leaf extract formulations, particularly the cream formulation, demonstrated superior efficacy in reducing psoriasis-like skin inflammation and restoring epidermal structure compared to allantoin based treatments and mometasone. These findings suggest that *Echinacea* derived bioactive compounds may represent promising candidates for the development of alternative or adjunctive therapies for inflammatory skin diseases.

Keywords: topical formulations, *Echinacea* leaf extract, psoriasis, rat model, herbal therapeutics

Acknowledgement: *Supported by TKP2021-EGA-19 and GINOP-2.3.4-15-2016-00002 projects.*

OL35

IDO1-driven metabolic and transcriptional programs slow migration and growth in breast cancer

Lilla Hornyák,[a,b] Zsolt Ráduly,[a] Katalin Erdélyi,[c] , Beáta Boros-Oláh,[a] Éva Nagy,[a] Zeina Esmandar,[a] Roland Tengölics,[d] Csilla Sajben,[d] Zsuzsanna Szabó,[e] Nikoletta Dobos,[e] Gábor Halmos,[e] Zsolt Karányi,[a,f] Csaba Hegedűs,[g] József Tóvári,[h] Péter Nagy,[c,h,i,j] Márton Miskei,[k] Lóránt Székvölgyi[a,b]

[a]*Momentum Genome Architecture and Recombination Research Group, Department of Molecular and Nanopharmaceutics, Faculty of Pharmacy, University of Debrecen, Debrecen, Hungary*
[b]*Doctoral School of Molecular Cell and Immune Biology, University of Debrecen, Debrecen, Hungary*
[c]*Department of Molecular Immunology and Toxicology and the National Tumor Biology Laboratory, National Institute of Oncology, Budapest, 1122, Hungary*
[d]*Metabolomics Laboratory, Core Facilities, HUN-REN Biological Research Centre, Szeged, Hungary*
[e]*Department of Biopharmacy, Faculty of Pharmacy, University of Debrecen, Debrecen, Hungary*
[f]*Department of Internal Medicine, Faculty of Medicine, University of Debrecen, Debrecen, Hungary*
[g]*Department of Medical Chemistry, Faculty of Medicine, University of Debrecen, Debrecen, Hungary*
[h]*Department of Oncology, Semmelweis University, Budapest, Hungary*
[i]*Chemistry Coordinating Institute, University of Debrecen, Debrecen, Hungary*
[j]*Department of Anatomy and Histology, HUN-REN–UVMB Laboratory of Redox Biology Research Group, University of Veterinary Medicine, Budapest, Hungary*
[k]*Department of Molecular Biotechnology and Microbiology, Faculty of Science and Technology, University of Debrecen, Debrecen, Hungary*

E-mail: lorantsz@med.unideb.hu, raduly.zsolt@med.unideb.hu

Indoleamine-2,3-dioxygenase 1 (IDO1) is a key regulator of tumor metabolism and immunity, yet pharmacological inhibition of its catalytic activity has yielded limited clinical benefit. We hypothesised that the prognostic impact of IDO1 is cancer-type dependent and that this context specificity may explain the discordance between biology and trial outcomes. We stratified human malignancies into adverse, favorable, and neutral prognostic classes based on the association between IDO1 expression and overall survival, identifying breast cancer as a favorable context. IDO1 was genetically enforced in breast cancer cell lines and xenograft models. Cellular phenotypes were assessed by migration assays and in vivo tumor growth analyses. Unbiased UPLC–MS/MS metabolomics and RNA sequencing were performed, followed by integrative multiomics analysis. Elevated IDO1 expression suppressed cell migration and significantly delayed tumor outgrowth in vivo. Metabolomic profiling revealed sustained tryptophan-to-kynurenine flux accompanied by a dual ATP/GTP deficit, pyrimidine depletion, and compensatory pentose-phosphate–mediated redox remodeling. Transcriptomic analysis demonstrated coordinated repression of extracellular matrix remodeling, cytoskeletal organization, and angiogenic programs. Multiomics integration linked these metabolic and transcriptional alterations to impaired migratory capacity and attenuated proliferation. These findings identify IDO1 as a context-dependent regulator of tumor progression and provide a mechanistic basis for the improved survival observed in IDO1-high breast cancer. The data support biomarker-guided, cancer-type–specific deployment of IDO1-directed therapies and caution against indiscriminate catalytic inhibition in contexts where IDO1 activity may be neutral or protective.

Acknowledgement: *This study was supported by the National Research, Development, and Innovation Office (Hungary) projects NKFIH-K-142137 (LSz), and NKFIH-K-137678 (MM), the Thematic Excellence Programme TKP2021-EGA-18 (LSz) and TKP2021-EGA-20 (Biotechnology) (GH) as part of the TKP2021-EGA scheme. The project was implemented with the support from the National Research, Development and Innovation Fund of the Ministry of Culture and Innovation under the National Laboratories Program (National Tumor Biology Laboratory (2022-2.1.1-NL-2022-00010)) and the Hungarian Thematic Excellence Program (under project TKP2021-EGA-44) Grant Agreements with the National Research, Development and Innovation Office. This project has received funding from the HUN-REN Hungarian Research Network (grant 1500207).*

OL36

Post-COVID otolaryngological syndrome and post-vaccine tinnitus

András Szilágyi,[a, b] Dávid Kovács,[c] Tamás József Batta,[c] Judit Szilvássy,[c] Balázs Sztanó,[c] Zoltán Papp,[c] Rita Kiss,[d] Béla Juhász,[a,d] Zoltán Szilvássy[a, d]

[a]*University of Debrecen, Doctoral School of Food Sciences, 4032, Debrecen, Hungary*
[b]*Semmelweis University, Otolaryngology Head and Neck Surgery, 1083, Budapest, Hungary*
[c]*University of Debrecen, Otolaryngology Head and Neck Surgery, 4032, Debrecen, Hungary*
[d]*University of Debrecen, Department of Pharmacology, 4032, Debrecen, Hungary*

E-mail: szilagyi.andras3@semmelweis.hu

Post-COVID syndrome frequently presents with otolaryngological manifestations, most commonly olfactory and gustatory dysfunctions, but also less commonly tinnitus and sensorineural hearing loss (SNHL) following infection or vaccination. This study aimed to evaluate socio-demographic and clinical factors influencing olfactory and gustatory recovery, with particular attention to physical activity, and to highlight challenges in managing auditory complications associated with COVID-19 vaccination. A cohort of 57 patients with confirmed COVID-19 infection and persistent olfactory and/or gustatory dysfunction (>1 month) was analyzed. Objective testing included Burghart Sniffin' Sticks and Taste Strips following exclusion of other causes. Treatment consisted of topical nasal corticosteroids, oral vitamin B complex, and Hummel's olfactory training, with a one-year follow-up and three control visits. Additionally, we report a case of a 79-year-old female who developed bilateral tinnitus after Sinopharm COVID-19 vaccination, assessed with audiometry and tinnitus handicap inventory (THI). Statistical analysis evaluated associations between epidemiological factors and Threshold-Discrimination-Identification (TDI) scores. The cohort consisted of 72.9% females, with a mean age of 41 years. Sex, BMI, and age were not associated with poorer olfactory outcomes. Early onset of olfactory dysfunction and regular physical activity were associated with significantly better TDI scores. Patients presenting with both olfactory and gustatory symptoms showed superior recovery compared to those with isolated olfactory dysfunction. Significant improvement in TDI scores was observed at one year. In contrast, the case of post-vaccination tinnitus demonstrated persistent high-frequency SNHL despite treatment with vitamin B complex and piracetam, with only slight improvement in THI score. Combined therapeutic strategies, including olfactory training and supportive pharmacological treatment, are effective in improving post-COVID olfactory and gustatory dysfunction, with physical activity emerging as a positive prognostic factor. However, auditory complications such as tinnitus following COVID-19 vaccination remain rare but challenging to manage, underscoring the need for early recognition and tailored therapeutic approaches.

Acknowledgement: *Supported by the GINOP-2.3.4-15-2016-00002, GINOP-2.3.4-15-2016-410 00002, GINOP-2.3.3-15-2016-00021 and TKP2021-EGA-19 projects.*

OL37

Survey of cardiopulmonary status and arrhythmia risk of patients who had a SARS-CoV-2 infection

Zoltán Szabó[a,b] Péter Kovács,[a,b] Veronika Sebestyén,[a,b] Lilla Végh[a,b]

[a]*Department of Emergency Medicine, Faculty of Medicine, University of Debrecen, 4032 Debrecen, Hungary*
[b]*Doctoral School of Health Sciences, University of Debrecen, 4032 Debrecen Hungary*

E-mail: szaboz.med@gmail.com

In 2019, the SARS-CoV-2 infection (severe acute respiratory syndrome coronavirus 2) originating from the Chinese city of Wuhan caused a pandemic that killed countless people. Post-COVID-19 syndrome affects up to 20% of patients, manifesting as multi-organ symptoms that persist beyond 4 weeks. Malignant arrhythmias and pulmonary embolism represent the two most critical, life-threatening complications. Understanding the underlying pathomechanisms and identifying reliable risk predictors are crucial for optimizing patient outcomes. The most important risk factors are age over 65, male gender, smoking, obesity and certain chronic diseases (hypertension and diabetes mellitus). In the case of patients belonging to this risk group, due to inflammation of the lungs and blood vessels, respiratory failure and heart rhythm disorders often develop, which can lead to sudden cardiac arrest.

In our study, which is based on retrospective data collection (N= 3521), prospective examination and follow-up (N=46) of patients treated at the Department of Emergency Medicine, Clinical Centre of the University of Debrecen, we analyzed the cardiopulmonary status of patients with SARS-CoV-19 infection. We assessed the cardiopulmonary condition of post-COVID patients based on physical and instrumental examinations and repeated the examinations after 3 months. We performed detailed laboratory biomarker analysis, echocardiography, and 24-hour Holter-ECG monitoring. We also determined the atrial (P wave interval (Pint), P wave dispersion (Pd)) and ventricular arrhythmia risk markers (QT interval (QTint), QT dispersion (QTd), T wave peak-to-end interval (Tpe) and arrhythmogeneity index (AIX)) based on 12-lead digital electrocardiography (ECG). Furthermore, we investigated the potential correlations between arrhythmia ECG markers and laboratory biomarkers.

Our findings demonstrate that both ventricular (QTint, QTd, Tpe, AIX) and atrial arrhythmia risk markers (Pint, Pd) increased among post-COVID syndrome patients compared to the healthy controls (N=35). ECG markers showed correlations with certain cardiac and inflammatory biomarkers, while no significant structural abnormalities were detected during echocardiography. We can conclude that the determined ECG and laboratory markers may be useful diagnostic tools in the follow-up of post-COVID patients and can be utilized in the early detection of increased arrhythmia risk in post-COVID population and ensure the possibility of immediate intervention.

Acknowledgement: *Project no. TKP2021-EGA-19 has been implemented with the support provided by the Ministry of Culture and Innovation of Hungary from the National Research, Development and Innovation Fund, financed under the TKP2021-EGA funding scheme.*

OL38

Comprehensive analysis of humoral and cellular immune responses induced by SARS-CoV-2 vaccines

Eszter Csoma,[a] György Hajas,[b] Zsófia Pénzes,[b] Attila Bácsi[b]

[a]*Department of Medical Microbiology, Faculty of Medicine, University of Debrecen, 4032, Debrecen, Hungary*
[b]*Department of Immunology, Faculty of Medicine, University of Debrecen, 4032, Debrecen, Hungary*

E-mail: etele@med.unideb.hu

Our aim was to investigate the humoral immune response induced by three vaccine types — mRNA, adenoviral vector-based, and inactivated virus-based vaccines — in individuals who had no confirmed history of SARS-CoV-2 infection and had received a complete vaccination protocol. Post-vaccination antibody levels were determined by comparing three methods: the Cobas Anti-SARS-CoV-2 test, which measures total immunoglobulins against the S1-RBD, and two assays measuring neutralizing antibodies: Medcaptain CLIA NAbs — Immu F6 and Snibe CLIA NAbs — Maglumi 800. The amount of neutralizing antibodies showed a good correlation with anti-S antibody levels, and based on the results, we determined a new optimal cut-off value for the anti-S total antibody assay used as a routine diagnostic test.

To achieve a more comprehensive assessment of vaccine-induced cellular immune responses, we developed a procedure that allows us not only to determine whether the blood of the examined individual contains memory T cells that recognize SARS-CoV-2 antigens and respond by producing interferon-γ, but also to precisely quantify the number of T cells reacting to viral antigens in the sample. As the first step of the assay, we performed an interferon-γ release assay (IGRA), and then carried out and optimized IFNγ ELISpot assays on cells obtained from the same test tube, for which we also established a positivity cut-off value. Using the developed assay procedures, we simultaneously examined the anti-SARS-CoV-2-specific humoral and T-cell immune responses of patients with chronic lymphocytic leukemia (CLL). We considered the assessment of cellular immune responses justified in these patients as well, since we detected a clear positive cellular immune response even in patients in whom antiviral antibodies were not detectable.

Acknowledgement: *This research was financed by the Thematic Excellence Program of the Ministry for Innovation and Technology in Hungary (TKP2021-EGA-19), within the framework of the thematic program of the University of Debrecen. Project TKP2021-EGA-19 was implemented with the support from the National Research, Development and Innovation Fund of Hungary, financed under the TKP2021-EGA funding scheme.*

OL39

COVID-19-associated coagulopathy in pregnancy: a prospective, case-control study

Zsuzsa Bagoly,[a] Eszter Lilla Tóth,[b] Rita Orbán-Kálmándi,[a] Tamás Deli,[b] Olga Török,[b] Linda Lóczi,[a] Judit Tóth,[c] Szabolcs Molnár,[b] Zoárd Tibor Krasznai[b]

[a]Department of Laboratory Medicine, Division of Clinical Laboratory Sciences,
[b]Department of Gynecology and Obstetrics,
[c]Department of Laboratory Medicine, University of Debrecen, Debrecen, Hungary

E-mail: toth.eszter.lilla@med.unideb.hu

Background. Coronavirus infection-19 (COVID-19) is associated with disturbed hemostasis balance. Little is known about COVID-19-associated hemostasis alterations in pregnancy and their associations with the clinical course.

Aims. To test hemostasis alterations in COVID-19-positive pregnant women as compared to non-infected pregnancies and correlate results with maternal and perinatal outcomes.

Methods. In this single-center observational case-control study, 102 women with acute COVID-19 infection at 24-40. gestational weeks (COVID-19+ group) and 96 healthy age- and gestational week-matched pregnant women (COVID-19- group) were enrolled. All women were outpatients with mild/no symptoms at admission. Acute infection was confirmed/ruled out using SARS-CoV-2 RT-PCR and/or antigen test. Blood taken on admission was analysed for markers of inflammation (CRP), D-dimer, fibrinogen, von Willebrand factor antigen, factor VIII (FVIII) and factor XIII (FXIII) activity, clot-lysis assay and thrombin generation. Detailed clinical parameters of pregnancy, labour and post-partum period were registered. Pregnancies were followed for 6 weeks after childbirth.

Results. In the COVID-19+ group, APTT was significantly prolonged, while PT, fibrinogen and D-dimer levels did not significantly different from the non-infected group. FVIII activity was significantly lower in the COVID-19+ group as compared to COVID-19- group. Similarly, FXIII activity was significantly reduced in COVID-19+ pregnant women vs. COVID-19- group. von Willebrand factor antigen levels were significantly higher in COVID-19 + pregnant women. Pregnancy-associated complications were observed in 5 COVID-19+ cases, with marked alterations of coagulation screening tests, clot-lysis assay and increased D-dimer. One newborn tested positive for SARS-CoV-2. No post-partum thrombotic events occurred.

Conclusions. In this cohort, third trimester COVID-19+ pregnancies were associated with reduced levels of FVIII and FXIII activity. In few cases, marked alterations of hemostasis and fibrinolysis balance occurred, which were accompanied with pregnancy complications.

OL40

A brief overview of the research group's work

Miklós Zrínyi[a]

[a]*Gyógyszer- és Élelmiszerfejlesztési Koordinációs Központ, 4032, Debrecen, Hungary*

E-mail: zrinyi.miklos@unideb.hu

Poster abstracts

P1

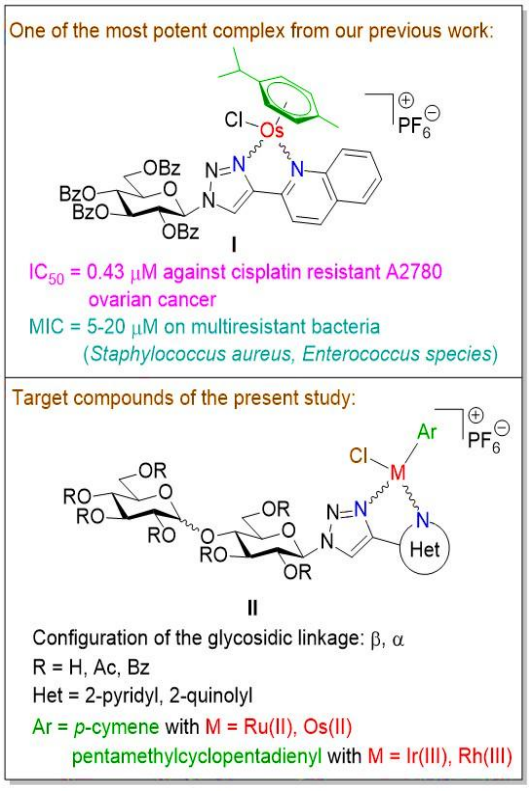
Synthesis and biological evaluation of half-sandwich type platinum-group metal complexes of *N*-β-D-disaccharidyl 1,2,3-triazoles

Alshimaa I. Zaki,[a,b] Éva Kerekes,[c] Adrienn Sipos,[c] István Kacsir,[a] Tünde Beáta Nagy,[d] Figueira Leticia Schroder,[d] Péter Buglyó,[e] Csongor Freytag,[d] Gábor Kardos,[d] Péter Bai,[c] Éva Bokor,[a] László Somsák[a]

[a]*Department of Organic Chemistry, Institute of Chemistry, University of Debrecen, 4032, Debrecen, Hungary*
[b]*Department of Chemistry, Faculty of Science, Mansoura University, 35516, Mansoura, Egypt*
[c]*Department of Medical Chemistry, Faculty of Medicine, University of Debrecen, 4032, Debrecen, Hungary*
[d]*One Health Institute, Faculty of Health Sciences, University of Debrecen, 4032, Debrecen, Hungary*
[e]*Department of Inorganic and Analytical Chemistry, University of Debrecen, 4032, Debrecen, Hungary*

E-mail: alshimaa.ibrahim@science.unideb.hu

Half-sandwich complexes of platinum-group metals are a large family of organometallic compounds with promising anticancer and antimicrobial activities. Earlier, we reported series of polyhapto arene/arenyl Ru(II), Os(II), Ir(III) and Rh(III) complexes with hetaryl-substituted *C*- and *N*-glycopyranosyl-azole-type N,N-bidentate ligands (azole = 1,2,3-triazole, 1,3,4- and 1,2,4-oxadiazole, isoxazole), several of which displayed antineoplastic and bacteriostatic potencies [1-4]. The structure-activity relationships (SAR) of the set have revealed that the nature of the proximal five-membered heteroring play a decisive effect on the biological activity. In addition, the highly hydrophobic *O*-protection of the sugar part is also a crucial factor in the potency [1-4]. The complexes of *N*-β-D-glucopyranosyl-1,2,3-triazoles represent one of the most effective subgroups, among which the (η^6-*p*-cymene)Os(II) complex with *O*-perbenzoylated 1-(β-D-glucopyranosyl)-2-quinolyl-1,2,3-triazole (**I**) displayed submicromolar cytostatic activity against cisplatin resistant A2780 ovarian cancer and also showed micromolar bacteriostatic effect against multiresistant Gram-positive bacteria [3]. For an extension of the SAR of this compound class on the test of the variability of the sugar part, the synthesis of complexes with other *N*-β-D-glycosidically linked 1,2,3-triazoles was envisaged. As part of this work, the replacement of the glucopyranosyl unit by disaccharidyl (maltosyl and cellobiosyl) moieties (**II**) have been accomplished. In the poster the synthesis of the new complexes and their biological results will be presented.



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P2

Synthesis of carbohydrate-containing 1,4-disubstituted triazoles and their evaluation as galectin inhibitors

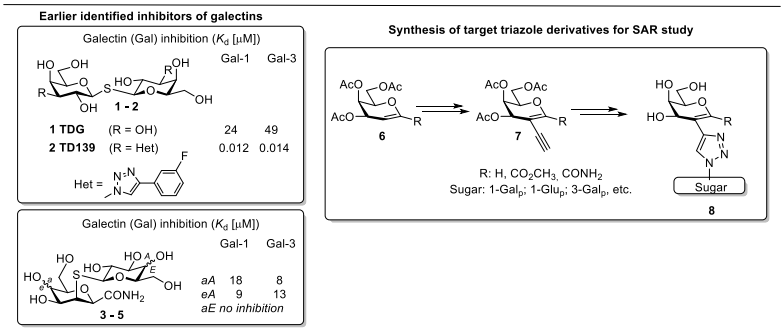
Éva Juhász-Tóth,[a] Dominik István Kocsi,[a] Balázs Nagy,[a,d] Norbert Ling,[a] Péter Posta,[a] Ágnes Homolya,[b] Ulf J. Nilsson,[c] László Somsák,[a] László Juhász[a]

[a]*Department of Organic Chemistry, University of Debrecen, PO Box 400, H-4002 Debrecen, Hungary*
[b]*Department of Pharmacuetical Chemistry, University of Debrecen, PO Box 400, H-4002 Debrecen, Hungary*
[c]*Department of Chemistry, Lund University, PO Box 124, SE-22100 Lund, Sweden*
[d]*Doctoral School of Chemistry, University of Debrecen, PO Box 400, H-4002 Debrecen, Hungary*

E-mail: toth.eva@science.unideb.hu

Galectins comprise a family of β-galactoside-binding proteins that crucially regulate immune responses, cellular recognition, and diverse pathologies, including cancer development and host–pathogen interactions. Among the 19 mammalian galectins discovered so far, 13 are expressed in humans [1]. Representative galectin inhibitors, including 1,1′-thiodigalactosides **1** and **2** [2] and 1,2-thioglycosides **3–5** [3], are illustrated in Scheme 1. Notably, the incorporation of a 1,2,3-triazole-linked aromatic group in **2** significantly boosts the binding affinity of the core scaffold [2].

The primary objective of this study was the design and synthesis of carbohydrate-functionalized 1,4-disubstituted triazole structures as potential galectin inhibitors. Utilizing 2-ethynyl-galactals **7** (prepared from precursor **6**) as the starting material, we accomplished the synthesis of pseudo-bisglycosyl-triazoles **8** through a copper-catalyzed azide–alkyne cycloaddition (CuAAC) reaction. Subsequent deacetylation under Zemplén conditions successfully yielded the target deprotected derivatives (Scheme 1).



Scheme 1: Earlier identified inhibitors of Gal-1 and Gal-3 and synthesis of target triazole derivatives

The established synthetic pathway provides a robust strategy for generating novel, structurally adaptable galectin inhibitor candidates. In vitro biological assays of the newly prepared compounds are currently underway at Lund University, and the resulting data are anticipated to offer deeper insights into the precise structural parameters governing galectin–glycan recognition.

Acknowledgements: *The research was supported by the National Research, Development and Innovation Office of Hungary under the projects K146147 (to L. S.) and 2024-1.2.3-HU-RIZONT-2024-00005 (to L. S.).*

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P3

Development and characterization of topical formulations containing combined *Artemisia annua* and *Curcuma longa*

Barbara Balogh,[a] Ágota Pető,[a] Boglárka Papp,[a] Krisztina Bodnár,[a] Ágnes Klusóczki,[a] Pálma Fehér,[a] Zoltán Ujhelyi,[b] Ildikó Bácskay,[a]

[a]*Department of Pharmaceutical Technology, Faculty of Pharmacy, University of Debrecen, 4400, Debrecen, Hungary*
[b]*Department of Industrial Pharmaceutical Technology, Faculty of Pharmacy, University of Debrecen, 4400, Debrecen, Hungary*

E-mail: bacskay.ildiko@pharm.unideb.hu

The application of plant-derived active compounds has gained increasing attention in the development of dermatological formulations, particularly for the treatment of inflammatory skin disorders [1]. *Artemisia annua* and *Curcuma longa* are well-known for their antioxidant and anti-inflammatory properties [2, 3]. However, limited literature data are available regarding their combined topical application. Therefore, the aim of our study was to develop and evaluate novel topical formulations containing a combination of these plant extracts, which may be effective in the management of inflammatory skin conditions. Six different formulations were prepared, including three ointments and three gels, all containing both plant extracts. During formulation development, various surfactants (Labrafil, Miglyol 840, and PEG 400) were applied, and their effects on the structural and physicochemical properties of the systems were investigated. The formulations were characterized by rheological analysis, texture profiling, and pH measurement to determine their suitability for dermal application. The most promising systems were further assessed for antioxidant activity using DPPH and CUPRAC assays, as well as for in vitro cytotoxicity on HaCaT keratinocyte cells. Anti-inflammatory effects were examined in a TNF-α-induced HaCaT model through the determination of IL-1β levels by ELISA. Distinct differences were observed between ointment and gel formulations regarding their mechanical and rheological properties. Ointments exhibited higher structural stability, whereas gels showed better spreadability and more favorable consistency. Most selected formulations maintained skin-compatible pH values and did not demonstrate cytotoxic effects. Antioxidant testing confirmed radical scavenging activity, while ELISA results supported anti-inflammatory potential. Overall, topical formulations combining *Artemisia annua* and *Curcuma longa* appear to be promising candidates for the management of inflammatory skin diseases.

Acknowledgement: *Project no. TKP2021-EGA-18 was implemented with the support provided by the Ministry of Culture and Innovation of Hungary from the National Research, Development and Innovation Fund, financed under the TKP2021-EGA funding scheme and by 2022-1.2.2-TÉT-IPARI-UZ-2022-00006 Common research and development of different prototypes containing natural herb extract for industrial utilisation. The scientific work/research and/or results publicised in this article were achieved with the sponsorship of Gedeon Richter Talentum Foundation in the framework of the Gedeon Richter Excellence PhD Scholarship of Gedeon Richter. Supported by the EKÖP-25-3-II University Research Scholarship Program of the Ministry for Culture and Innovation, from the National Research, Development and Innovation Fund.*

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P4

Lipophilic modification of teicoplanin with natural steviol and cannabinoid derivatives

Benedek Máté Nagy,[a] Gergely Tóth,[a,b,c] Ferenc Dániel Petróczi,[a,b,d] Eszter Ostorházi,[e] Zsolt Szakonyi,[f] Anikó Borbás,[a] Pál Herczegh,[a] Ilona Bereczki[a]

[a]*University of Debrecen, Department of Pharmaceutical Chemistry, 4032, Debrecen, Hungary*
[b]*University of Debrecen, Doctoral School of Pharmaceutical Sciences, 4032, Debrecen, Hungary*
[c]*Science Port Kft.,300 Karcag, Hungary*
[d]*GlycOptim Kft., 4032, Debrecen, Hungary*
[e]*Semmelweis University, Department of Medical Microbiology, 1089, Budapest, Hungary*
[f]*University of Szeged, Institute of Pharmaceutical Chemistry, 6720, Szeged, Hungary.*

E-mail: nagybeni04@mailbox.unideb.hu; bereczki.ilona@pharm.unideb.hu

Glycopeptide antibiotics (e.g., vancomycin, teicoplanin) are natural or semi-synthetic compounds that inhibit cell wall synthesis in Gram-positive bacteria. Their clinical application is restricted to the hospital treatment of severe infections caused by multi-drug resistant strains, often serving as a last-resort defense. However, antimicrobial resistance represents a rapidly escalating global threat, which is projected to become a leading cause of mortality worldwide within the next 20–25 years. Unfortunately, a certain degree of resistance has already emerged against glycopeptide antibiotics, necessitating the development of novel derivatives with enhanced efficacy to combat these resistant bacterial strains.

We have previously demonstrated that conjugating teicoplanin pseudoaglycone with lipophilic groups yields derivatives with potent antibacterial and/or antiviral activities [1,2]. Our previous findings also indicated that a higher lipophilicity of the conjugated moiety correlates with increased cytotoxicity [3]. To overcome this limitation, we successfully coupled natural, lipophilic, non-toxic molecules to the teicoplanin pseudoaglycone core, resulting in highly effective yet non-toxic conjugates [4]. Building upon this strategy, our current objective was to synthesize novel derivatives by linking lipophilic steviol and cannabinoid (CBD, CBG) derivatives to teicoplanin pseudoaglycone scaffolds. Some of the newly synthesized derivatives demonstrated excellent efficacy against various Gram-positive bacterial strains.

Acknowledgement: *This research was supported by the National Research, Development and Innovation Office of Hungary FK 142315, the KDP-2023 Program, and the EKÖP-KDP-2025 University Research Scholarship Program – Cooperative Doctoral Program of the Ministry for Culture and Innovation from the Source of the National Research, Development and Innovation Fund. It was also supported by the „Debrecen Venture Catapult Program" EFOP-3.6.1-16-2016-00022, the PhD Excellence Scholarship from the Count István Tisza Foundation for the University of Debrecen.*

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P5

Synthesis of guanidine-based molecules via desulfonative smiles rearrangement

Devesh Panchal,[a] Dharmender Kumar,[a] Priyamvada Singh[a]

[a]*Department of Chemistry, Miranda House, University of Delhi,110007, Delhi, India*

E-mail: priyamvada.singh@mirandahouse.ac.in

Guanidine-containing compounds are highly privileged structural motifs in medicinal chemistry, exhibiting diverse biological activities including antimicrobial, antiviral, and anticancer properties [1–3]. However, classical methods for guanidine synthesis often rely on preactivated substrates or harsh reaction conditions, limiting functional-group tolerance [4]. In recent years, rearrangement-based strategies have emerged as powerful alternatives for C–N bond formation and the construction of nitrogen-rich frameworks. The Smiles Rearrangement, an intramolecular nucleophilic aromatic substitution process, has proven to be a versatile platform for aryl transfer reactions [5]. Desulfonative variants of this transformation are particularly attractive, as sulfonyl groups can act as traceless activating and leaving groups, thereby promoting efficient aryl migration under mild, transition-metal-free conditions. Herein, we report a novel desulfonative Smiles Rearrangement approach for the synthesis of guanidine derivatives. The developed methodology demonstrates good functional-group tolerance across a range of substrates, though the electronic effects of aromatic substituents influence reactivity. The synthetic utility of this approach was validated through systematic optimization studies and detailed mechanistic investigations. NMR studies support an intramolecular nucleophilic aromatic substitution mechanism. This work provides a practical and concise route to structurally diverse guanidine frameworks with potential medicinal applications. A detailed discussion of their synthesis, characterization, and biological evaluation will be presented.

Acknowledgement: *The authors acknowledge the financial support received from ANRF, Government of India (CRD/2022/000580).*

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P6

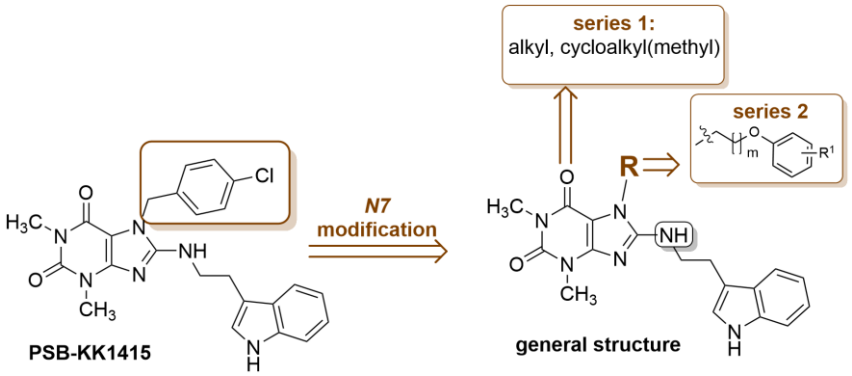
Search for agonists of the orphan G protein-coupled receptor GPR18

Dorota Łażewska,[a] Andhika B. Mahardhika,[b] Ewelina Honkisz-Orzechowska,[a] Michał Załuski,[a] Maria Kaleta,[a] Filomena Perri,[b] Grzegorz Baran,[a] Christa E. Müller,[b] Katarzyna Kieć-Kononowicz[a]

[a] *Department of Chemical Technology and Biotechnology of Drugs, Faculty of Pharmacy, Jagiellonian University Medical College in Kraków, ul. Medyczna 9, 30-688 Kraków, Poland*
[b] *Pharmaceutical Institute, Department of Pharmaceutical & Medicinal Chemistry, University of Bonn, An der Immenburg 4, D-53121 Bonn, Germany*

E-mail: dorota.lazewska@uj.edu.pl

GPR18 is an orphan receptor mainly found in tissues and cells associated with the immune system and in cancer cells [1]. However, the absence of potent and selective ligands limits the pharmacological characterisation of this receptor. We recently described a new class of GPR18 agonists [2]. Among them, the compound **PSB-KK1415** had the highest potency with an EC_{50} of 19 nM. Currently, **PSB-KK1415** is the most potent known GPR18 agonist, displaying >25-fold selectivity vs both CB receptor subtypes and the related orphan receptor GPR55. Continuing our research in this area, we designed and synthesised a series of compounds based on **PSB-KK1415** with modification of substituents at position 7 of the xanthine core (*Scheme 1*).



Scheme 1. *Structure of* ***PSB-KK1415*** *and planned modifications.*

The activity of the new compounds at the human GPR18 was evaluated using a β-arrestin recruitment assay, and EC_{50} values were determined. The most potent compounds were then examined for their selectivity against cannabinoid receptors and GPR55. In addition, potential cytotoxic effects of the lead compounds on neuronal, hepatic, and microglial cells were assessed after 72 h of incubation using the MTS assay. These novel ligands are valuable tools for target validation studies and further development of GPR18 agonists as novel therapeutic drugs.

Acknowledgement: *This research was in part funded by the National Science Centre, Poland, under grants: UMO-2021/43/B/NZ7/01938 and UMO-2021/43/D/NZ3/01440.*

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P7

Galectin-8: Moving from inhibition toward targeted protein degradation

Edvin Purić,[a] Lara Smrdel,[b] Katarina Miš,[c] Sergej Pirkmajer,[c] Ulf J. Nilsson,[d] Martina Gobec,[b] Marko Anderluh,[a]

[a]*Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Ljubljana, 1000, Ljubljana, Slovenia*
[b]*Department of Clinical Biochemistry, Faculty of Pharmacy, University of Ljubljana, 1000, Ljubljana, Slovenia*
[c]*Institute of Pathophysiology, Faculty of Medicine, University of Ljubljana, 1000, Ljubljana, Slovenia*
[d]*Department of Chemistry, Centre for Analysis and Synthesis, 221 00 Lund, Sweden*

E-mail: edvin.puric@ffa.uni-lj.si

Galectin-8, a member of the tandem-repeat class of galectins, plays a central role in numerous physiological processes, including cell adhesion, proliferation, signaling, autophagy, and differentiation. It is also involved in a range of pathological conditions such as fibrosis, cancer, and cardiovascular diseases, making it an attractive but challenging therapeutic target [1]. Conventional small-molecule inhibitors typically operate via an occupancy-driven mechanism by binding to one of the carbohydrate recognition domains (CRDs) of galectin-8. However, these ligands often suffer from limited potency and selectivity, commonly exhibiting dissociation constants in the low micromolar range, which constrains their therapeutic applicability [2,3].

To overcome these limitations, we pursued an alternative strategy aimed at depleting intracellular galectin-8 levels. Proteolysis-targeting chimeras (PROTACs) are heterobifunctional molecules composed of a ligand for the protein of interest, an E3 ligase-recruiting ligand, and a linker, and function through an event-driven mode of action that induces protein degradation [4]. In our study, we designed and synthesized a small library of PROTACs incorporating high-affinity ligands for the N-terminal domain of galectin-8 (Gal-8N), coupled with either cereblon (CRBN)- or von Hippel-Lindau (VHL)-recruiting ligands via appropriate linkers.

The binding affinities of our PROTACs for galectin-3 and -8N were first evaluated using a fluorescence polarization assay. Subsequently, their ability to induce degradation of both galectins was assessed in MDA-MB-231 and HUVEC cells. The most active degrader was further characterized in concentration-dependent degradation studies, confirming its capacity to effectively reduce intracellular galectin-8 levels [5].

To the best of our knowledge, our work represents the first application of PROTAC technology to galectin-8, introducing a new paradigm for targeting this protein and subsequently expanding the scope of galectin-directed therapeutic strategies.

Acknowledgement: *The financial support of this work from Slovenian Research Agency (Grant P1-0208 and 55895) is gratefully acknowledged. COST actions CA18103 (Innogly) and CA18132 (GlycoNanoPROBES) are also gratefully acknowledged.*

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P8

Septins couple calcium signalling to mitochondrial metabolism during chondrogenesis: an isoform-selective pharmacological dissection

Krisztián Zoltán Juhász,[a] Nawar Mohammad,[a] Roland Takács[a]

[a]*Department of Anatomy, Histology and Embryology, Faculty of Medicine, University of Debrecen, Debrecen, Hungary*

E-mail: juhasz.krisztian@anat.med.unideb.hu

Developing chondrocytes must coordinate Ca^{2+}-driven differentiation signals with a tightly constrained, hypoxia-adapted energy metabolism, yet the machinery linking these two systems remains poorly defined. Septins, the fourth component of the cytoskeleton, scaffold the endoplasmic reticulum–plasma membrane junctions that govern store-operated Ca^{2+} entry (SOCE), while the SEPT4/ARTS isoform localizes to mitochondria, making the family a candidate integrator of the calcium–mitochondrial axis during chondrogenesis. We tested this in primary chicken limb-bud micromass cultures using an isoform-resolving pharmacological wedge: broad-spectrum forchlorfenuron (FCF, 200 µM), which also inhibits SEPT4/ARTS, versus the SEPT6-preferring inhibitor REM-127 (0.3–3 µM), which largely spares it.

Broad-spectrum septin inhibition collapsed chondrogenesis across every readout. Cartilage matrix (DMMB metachromasia) fell to 67–84% of control, chondrogenic marker genes (Sox9, Col2a1, Acan, Hapln1) to ~15%, and proliferation and collagen synthesis to 20–35%, whereas the pluripotency marker PouV rose ~2-fold. Extracellular flux analysis showed a near-complete loss of maximal (FCCP-stimulated) mitochondrial respiration (−86%) together with a rise in glycolysis (ECAR +76%); this metabolic switch reconciles the paradoxical increase in MTT signal (~140%), indicating reprogramming rather than cytotoxicity.

In contrast, isoform-selective inhibition with REM-127 left cartilage matrix, metabolic activity, and the core chondrogenic and SOCE gene programs essentially unchanged. Notably, REM-127 selectively and dose-dependently reduced the hypertrophic marker Col X (COL10A1) by ~45% within the day 3–5 window, without compromising the chondrogenic program.

Together, these data indicate that a specific septin isoform, most likely SEPT4/ARTS, gates chondrogenesis by coupling Ca^{2+} signalling to mitochondrial metabolism. Selective targeting can down-modulate the hypertrophic shift, a key failure mode in cartilage tissue engineering, without disrupting matrix formation, highlighting septins as a promising integrative target for cartilage biology and repair.

Acknowledgement: *This research was supported by the EKÖP-25-4 University Research Fellowship Program of the Ministry for Culture and Innovation from the source of the National Research, Development and Innovation Fund, Hungary, awarded to RT (EKÖP-25-4-II-DE-249). RT also acknowledges financial support from the European Cooperation in Science and Technology COST Association Action CA21110 – Building an open European Network on OsteoArthritis research (NetwOArk); https://www.cost.eu/actions/CA21110/).*

P9

Comparison and evaluation of the efficacy of topical drug formulations containing diclofenac

Krisztina Bodnár,[a] Gergő Kis,[b] Liza Józsa[a,b]

[a]*Department of Pharmaceutical Technology, Faculty of Pharmacy, University of Debrecen, 4002, Debrecen, Hungary*
[b]*Doctoral School of Pharmaceutical Sciences, University of Debrecen, 4032 Debrecen, Hungary*

E-mail: bodnar.krisztina@pharm.unideb.hu

The appropriate selection of a dosage form intended for dermal application is of fundamental importance for therapeutic success, as it directly influences drug absorption, bioavailability and, consequently, treatment efficacy [1]. The skin, as an organ suitable for drug delivery, possesses distinctive anatomical and physiological properties that substantially determine the behaviour and performance of different formulations. In addition to therapeutic effectiveness, the choice of dosage form may also influence patient comfort, treatment adherence and treatment-related costs [2]. The aim of the research was to perform a comparative investigation of different dermal dosage forms containing diclofenac sodium, gel, cream and foam, with regard to drug release, bioavailability, toxicity and anti-inflammatory activity. The three formulations were subjected to texture analysis. Drug release and membrane penetration were investigated using Franz diffusion cells, while quantitative determination was carried out by UV–Vis spectrophotometry. Biocompatibility was assessed by MTT-based cytotoxicity studies on the human keratinocyte HaCaT cell line. The in vitro anti-inflammatory activity was evaluated on HaCaT cells by determining human TNF-α and IL-1β levels using ELISA. Based on the results of the Franz diffusion cell studies, the foam formulation exhibited the most favourable penetration profile, followed by the cream and then the gel. The MTT assays confirmed that all three formulations displayed adequate biocompatibility; however, a greater reduction in cell viability was observed in the case of the cream and gel, which may presumably be attributed to the composition of the excipients used. Evaluation of anti-inflammatory activity demonstrated that treatment with the foam produced the most pronounced anti-inflammatory effect, whereas no significant difference could be detected between the effects of the cream and gel formulations. Based on our findings, it may be concluded that the diclofenac sodium-containing foam formulation proved to be the most advantageous in terms of drug release, bioavailability, biocompatibility and anti-inflammatory activity. The study highlights that the type of dosage form itself may represent a decisive factor in optimising the therapeutic performance of dermal formulations.

Acknowledgement: *Supported by the eköp-25-3-II university research scholarship program of the ministry for culture and innovation from the source of the national research, development and innovation fund. This research was funded by TKP2021-EGA-18, implemented with the support provided by the Ministry of Culture and Innovation of Hungary from the National Research, Development and Innovation Fund, financed under the TKP2021-EGA funding scheme, and by 2022-1.2.2-TÉT-IPARI-UZ-2022-00006 for the common research and development of different prototypes containing natural herb extract for industrial utilization.*

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P10

Glycopeptide antibiotics derivates antiviral activity against Alphaviruses on different cell lines

Krisztina Rebeka Leiner,[a,c] Ilona Bakai-Berecki,[a,b] Zoltán Kopasz,[a,c] Kornélia Bodó,[a] Eszter Szabó,[a] Anikó Borbás,[a,b] Anett Kuczmog,[a,c]

[a]*National Laboratory of Virology, Szentágothai Research Centre, Ifjúság útja 20, H-7624 Pécs, Hungary*
[b]*Department of Pharmaceutical Chemistry, University of Debrecen, Egyetem tér 1, H-4032 Debrecen, Hungary*
[c]*Institute of Biology, Faculty of Sciences, University of Pécs, Ifjúság útja 6, H-7624 Pécs, Hungary*

E-mail: leiner.krisztina@pte.hu

Thousands of viruses capable of infecting humans circulate worldwide, yet effective vaccines and specific antiviral therapies are available for only a limited number of them. Among the understudied arboviral pathogens are Sindbis virus (SINV) and O'nyong-nyong virus (ONNV), two mosquito-borne members of the Alphavirus genus. Although these viruses have a lower global health burden than major arboviruses such as Chikungunya, Dengue, or Zika viruses, they remain capable of causing outbreaks and debilitating febrile illnesses characterized by rash, arthralgia, and prolonged fatigue. Moreover, due to their close phylogenetic relationship to Chikungunya virus and their suitability for handling under biosafety level 2 (BSL-2) conditions, SINV and ONNV represent valuable surrogate models for studying alphavirus biology and for the identification of novel antiviral compounds. In the absence of licensed vaccines or specific antiviral therapies against these viruses, the development of effective antiviral strategies remains an important research objective.

In this study, we investigated the antiviral efficacy of synthetic antibiotics and their derivatives against Sindbis and O'nyong-nyong viruses, encompassing a total of 26 compounds. These included the initial compounds, namely teicoplanin, ristocetin, and vancomycin, alongside their derivatives. All experiments were conducted in vitro utilizing Vero E6 and Hek-293 cell lines. Following cytotoxicity assessment, we determinde the titer of the viruses with Plaque assay on Vero E6 cells, and with TCID50 on Hek.293 cells, then we optimised the infection itself, and the antiviral potential of the compounds was evaluated through microscopic analysis and the MTT assay. Our findings revealed the different activity of the compound throughout different cell lines. Notably, among the 26 compounds, one of the ristocetine derivates (ERJ-552) exhibited exceptional antiviral properties against on both cell types and both viruses. Subsequent investigations were undertaken to elucidate its mechanism of action through further experimentation. Utilizing a time addition assay, we approximated the precise window during the infection cycle wherein the compound exerts its antiviral effects.

P11

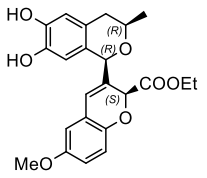
Synthesis and stereochemical investigation of axially chiral biaryls containing (1*R*,3*R*)-1-arylisochroman subunit

Muhammad Raza Saleem,[a] Krisztián Cserepes,[a] Attila Mándi,[a] Tibor Kurtán[a]

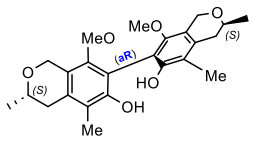
[a]*University of Debrecen, Faculty of Science and Technology, Institute of Chemistry, Department of Organic Chemistry, 4032 Debrecen, Hungary*

E-mail: muhammadrazasaleem@mailbox.unideb.hu

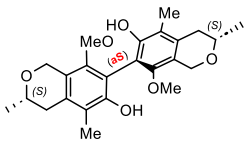
An optically active synthetic isochroman-2*H*-chromene conjugate JE-133 (**1**), synthesized in the research group, was found to prevent SH-SY5Y neuroblastoma cells from hydrogen peroxide (H_2O_2)-induced cell death [1]. Recently, anti-inflammatory activity of our conjugate was also observed on microglia cells and we prepared all the eight stereoisomers and provided 2.0 g enantiopure sample of **1** for *in vivo* testing in a novel stroke model [2]. Motivated by our stereochemical analysis of isolated axially chiral *bis*-isochromans [3], we achieved the first synthesis of optically active biaryl-type heterodimeric *bis*-isochromans **2** containing both axial and central chirality elements [4]. Compound **3** showed good antibacterial activity against methicillin-resistant *Staphylococcus aureus*, and the synthesis, structural analysis and antibacterial activity of *bis*-isochromans were disclosed in a patent [5].



JE-133 **1**



penicisteckin C **2a**[4]



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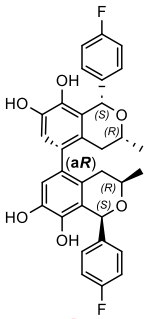

3[5]

Inspired by our synthesis of axially chiral biaryls, we envisioned the stereoselective synthesis of axially chiral isochroman-benzoflavone and isochroman-benzoflavanone conjugates. A (1*R*,3*R*)-1-aryl-5-iodoisochroman derivative is subjected to a Suzuki-Miyaura biaryl cross-linking reaction with a modified 1-naphthol reagent to stereoselectively prepare 5,4'-coupled isochroman-1-naphthol hybrids containing axial and central chirality elements. We investigated the formation of a chalcone structural element with various benzaldehydes on the 1-naphthol unit before and after the biaryl coupling and performed cyclization reactions to form a benzoflavanone or benzoflavone subunit. In the cyclization reactions of chalcones, 5,6'-linked isochroman-benzo[h]flavone(flavanone) conjugates were prepared, containing central and axial chirality elements. We performed ECD, VCD measurements and DFT calculations to determine the configurations of central and axial chirality elements. *In vitro* pharmacological assays are in progress to identify antibacterial and antiproliferative activities.

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P12

An efficient synthesis of pyridine-based thioamides using elemental sulphur in aqueous medium

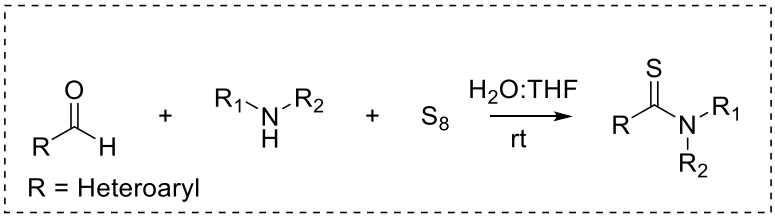
Parul Panwar,[a] Khushi Biswas,[a] Ankush Gupta[a] and Brijesh Rathi[a]

[a]*Laboratory For Translational Chemistry & Drug Discovery, Department of Chemistry, Hansraj College, University of Delhi, Delhi- 110007, India*

E-mail: brijeshrathi@hrc.du.ac.in

Pyridine-based thioamides are an important class of sulphur-containing heterocycles with broad pharmacological potential [1,2]. Previous reported synthesis for thioamide synthesis often includes harsh reaction conditions, metal catalysts, toxic solvents, and the additional activating reagents [3]. Herein, we report an efficient approach through a water-mediated direct thioamidation for the synthesis of pyridine-based thioamide derivatives. This devised methodology represents an extension of previous reported work in which thioamides are synthesized by aldehydes derivates [4]. The protocol utilizes pyridine aldehydes, elemental sulphur, and diverse amine partners under mild reaction conditions without the use of catalysts, oxidants, or additional activating agents, providing an eco-friendly alternative to the conventional process of thioamide synthesis.

The developed protocol showed broad substrate scope and desired thioamide derivatives were obtained in moderate to excellent yields. The results of this study indicate that pyridine-based thioamides could be useful scaffolds for future medicinal and anti-tubercular studies.



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P13

Use of cyclodextrins as comprehensive series of reliable collision cross section calibrants in ion mobility–mass spectrometry

Péter Soma Szakály,[a,b,c] Viktória Goldschmidt Gőz,[a] Dávid Papp,[a,b] Erzsébet Varga,[c] Gitta Schlosser[a]

[a]*MTA-ELTE Lendület (Momentum) Ion Mobility Mass Spectrometry Research Group, ELTE Eötvös Loránd University, Institute of Chemistry, Department of Analytical Chemistry, H-1117, Budapest, Hungary*
[b]*Hevesy György PhD School of Chemistry, ELTE Eötvös Loránd University, Institute of Chemistry, H-1117, Budapest, Hungary*
[c]*CycloLab Cyclodextrin Research and Development Laboratory Ltd., H-1097, Budapest, Hungary*

E-mail: soma.szakaly@cyclolab.hu, szsoma@student.elte.hu

Ion mobility–mass spectrometry (IM–MS) has become an increasingly important analytical platform for the structural characterization and identification of biomolecules and bioactive compounds through the determination of collision cross section (*CCS*) values. *CCS* provides structural information that supports molecular annotation in complex biological and pharmaceutical samples. In travelling wave ion mobility spectrometry (TWIMS, TW) instruments, such as the Waters SELECT SERIES Cyclic IMS, accurate *CCS* determination relies on appropriate calibration strategies [1]. Previous studies have demonstrated that ^{TW}*CCS* accuracy can strongly depend on the molecular class of the calibrants, highlighting the need for application-specific calibration approaches [2]. Cyclodextrins (CDs) are cone-shaped cyclic oligosaccharides widely used in pharmaceutical formulations, drug delivery systems, host–guest chemistry, and biomedical applications due to their ability to form inclusion complexes with a broad range of therapeutic compounds [3]. Despite their growing relevance in life sciences and medicinal chemistry, only limited *CCS* data are currently available for CDs [4-5].

In this work, we introduce ^{TW}*CCS* calibration series composed of single-isomer CD derivatives spanning a *CCS* range of 280–430 Å² in both positive and negative ionisation modes. The performance of the CD-based calibration series was systematically compared with calibration sets originating from other molecular classes for the analysis of structurally diverse CD derivatives. ^{TW}*CCS* values were obtained from single-pass TWIMS measurements and evaluated against experimentally determined drift tube *CCS* (^{DT}*CCS*) reference data. Our results demonstrate that molecular class matching between calibrants and analytes is essential for achieving high *CCS* accuracy in CD analysis. The CD-based calibration series consistently produced the most reliable ^{TW}*CCS* values in both ionisation modes, supporting more confident structural characterization of cyclodextrin-containing systems. Furthermore, we provide a comprehensive *CCS* database for CDs that may facilitate future IM–MS applications in pharmaceutical research, drug formulation studies, and the analysis of supramolecular and biomolecular host–guest interactions.

Acknowledgement: *Project No. KT-2023-900-I1-00000975/0000003 has been implemented with the support provided by the Ministry of Culture and Innovation of Hungary from the National Research, Development and Innovation Fund, financed under the KDP-2023 funding scheme.*
This project was supported by the Lendület (Momentum) Program of the Hungarian Academy of Sciences (HAS, MTA) and by the SNN 148580 project implemented with the support provided by the Ministry of Innovation and Technology of Hungary from the National Research, Development and Innovation Fund, financed under the SNN_24 funding scheme, and by the Slovenian Research and Innovation Agency (ARIS).

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P14

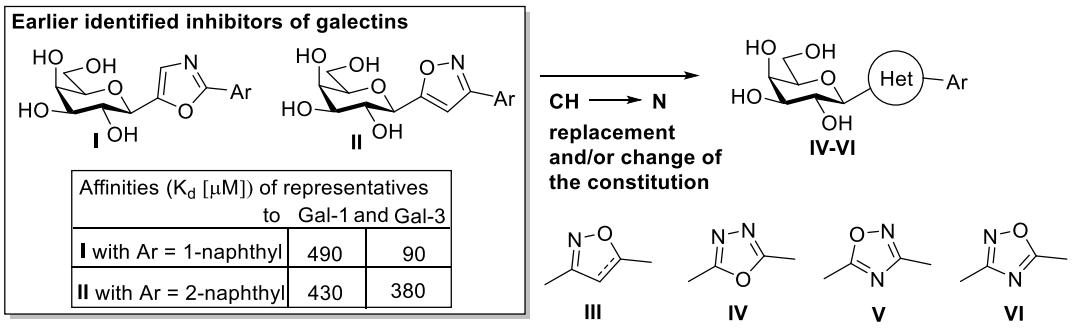
Synthesis and biological evaluation of (β-D-galactopyranosyl)oxadiazole, -isoxazole, and -isoxazoline derivatives targeting galectins

István Kacsir,[a] Samreen Saifi,[a,b] Ágnes Homolya,[a] Tímea Kaszás,[a] László Juhász,[a] Éva Juhász-Tóth,[a] Bence Szakács,[a,b] Sándor Kun,[a] Ulf J. Nilsson,[c] László Somsák,[a] Éva Bokor,[a] Marietta Tóth[a]

[a]*Department of Organic Chemistry, University of Debrecen, PO Box 400, H-4002 Debrecen, Hungary*
[b]*Doctoral School of Chemistry, University of Debrecen, PO Box 400, H-4002 Debrecen, Hungary*
[c]*Department of Chemistry, Lund University, PO Box 124, SE-22100 Lund, Sweden)*

E-mail: toth.marietta@science.unideb.hu, saifi.samreen@science.unideb.hu

Galectins constitute a family of galactoside-binding lectins, comprising 19 mammalian and 13 human subtypes [1a]. Among these, galectin-1 and -3 are the most extensively characterized; galectin-3 exhibits near-ubiquitous expression, whereas galectin-1 is predominantly localized in immune, muscle, and neuronal tissues, as well as the kidneys [1a]. These proteins modulate a wide array of intra- and extracellular functions, such as cell adhesion, migration, and apoptosis, and host defense. Because of these roles, they are implicated in several diseases such as idiopathic pulmonary fibrosis (IPF), inflammation, cancer, and autoimmune disorders [1b]. Since their natural ligands are glycoconjugates, therapeutic research focuses on carbohydrate-based inhibitors, including modified saccharides and thiodigalactoside derivatives. Notably, the galectin-3-selective TD139 has completed phase II clinical trials for IPF [2]. Previous studies evaluated *C*-galactopyranosyl heterocycles, specifically 2-aryl-5-oxazoles **I** and 3-aryl-5-isoxazoles **II**, as inhibitors. While oxazoles **I** showed favorable affinity and selectivity for galectin-3, isoxazoles **II** lacked selectivity [3]. To further explore structure–activity relationships, this study evaluates novel *C*-galactopyranosyl heterocycles against galectin-1 and -3. Oxadiazoles **IV**, **V** and **VI** were synthesized to investigate the impact of replacing the CH unit in compounds **I** and **II** with nitrogen. Additionally, previously synthesized isoxazoles and isoxazolines **III** [4] were evaluated as constitutional isomers of the isoxazole moiety in compounds **II**.



Scheme 1: Earlier identified *C*-β-D-galactopyranosyl azoles (**I** and **II**) as inhibitors of galectin-1 and galectin-3, and target compounds of this work (**III-VI**) for SAR study

Acknowledgement: *The research was supported by the National Research, Development and Innovation Office of Hungary under the projects PD 142641 (to T. K.), K146147 (to L. S.) and 2024-1.2.3-HU-RIZONT-2024-00005 (to L. S.).*

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P15

Codon usage analysis of influenza A virus

Shilpa[a], Brijesh Rathi[b], Mansi Verma[a]

[a]*Department of Zoology, Hansraj College, University of Delhi, 110007, Delhi, India*
[b]*Laboratory For Translational Chemistry & Drug Discovery, Department of Chemistry, Hansraj College, University of Delhi, Delhi- 110007, India*

E-mail: mansiverma@hrc.du.ac.in

Influenza A virus (IAV) is a significant global health challenge due to its elevated mutation frequency, ranging from 1.8-8.4 × 10^{-3} substitutions per site per year, along with frequent antigenic drift and antigenic shift, which facilitate rapid host adaptation and recurrent pandemic emergence [1-2]. Previous studies on codon usage bias have primarily focused on certain strains and individual genomic segments, while a comprehensive segment-wise evaluation across all eight genomic segments remains limited. In this study, 17,848 complete coding sequences representing 103 IAV strains derived from avian, human, swine and other hosts were retrieved from NCBI Nucleotide Database and analyzed using relative synonymous codon usage (RSCU), effective number of codons (ENc), neutrality plots, parity rule 2 (PR2) analysis, codon adaptation index (CAI), and tRNA adaptation index (tAI). Genome-wide analysis showed a strong preference for A/U ending codons, while G/C-ending and CpG-containing codons were significantly suppressed. Codons such as ACA, GGA, GCA and UCA preferred while CGG, ACG, CGU and UCG were underrepresented, likely suggesting adaptation for host immune evasion through reduced ZAP-mediated antiviral targeting. ENc-GC3 plot revealed that most sequences fell below wright's curve, indicating that natural selection is the major force shaping codon usage. Neutrality plot revealed that PB1, PB2, HA, NP and MP are evolutionary more conserved, whereas PA, NA and NS segments exhibit greater mutational pressure and adaptive potential. PR2 analysis revealed a strong adenine bias at the third codon position across most segments. CAI-ENc relationships highlight the host-specific translational adaptation particularly in HA and NA segments, particularly in HA and NA segments, indicating codon remodeling during interspecies transmission. Host- adaptive codon usage patterns may aid the development of vaccines, attenuation strategies and codon optimization-based antivirals targeting conserved IAV segments [3-4]. Collectively, the findings indicate natural selection and host specific translational optimization as key drivers of IAV evolution.

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P16

Antiviral activity against wild-type Lloviu cuevavirus in a bat-derived cell model

Zoltán Kopasz,[a,b] Levente Láng,[a] Ágota Ábrahám,[a,b] Eszter Szabó,[a] Anett Kuczmog,[a,b] Gábor Kemenesi[a,b]

[a]*National Laboratory of Virology, Szentágothai Research Centre, University of Pécs, Pecs, Ifjúság útja 20, 7624, Hungary*
[b]*Faculty of Sciences, Institute of Biology, University of Pécs, Pecs, Ifjúság útja 6, 7624, Hungary*

E-mail: kopasz.zoltan@pte.hu

Lloviu cuevavirus (LLOV) is a filovirus circulating in European bat populations that replicates efficiently in human and bat-derived cells, although no confirmed human infections have been reported to date. Experimental data on antiviral susceptibility remain extremely limited, with only a single study performed using recombinant LLOV systems.

Antiviral activity was examined using infectious wild-type Lloviu cuevavirus (LLOV) in SuBK12-08 bat kidney cells derived from relative Miniopterus species. Nucleoside-based RNA-dependent RNA polymerase inhibitors (remdesivir and obeldesivir) and semisynthetic glycopeptide antibiotics, including teicoplanin and ristocetin derivatives, were evaluated in independent experimental settings. Viral replication and compound-associated cytotoxicity were assessed using plaque reduction assays, RT–qPCR quantification of extracellular viral RNA, and longitudinal live-cell imaging over a nine-day infection period.

Remdesivir inhibited LLOV replication in SuBK12-08 cells but exhibited higher cytotoxicity; however, its effective antiviral concentration range remained comparable. Obeldesivir did not display increased antiviral potency relative to remdesivir, but showed improved cellular tolerability, resulting in a higher selectivity index and absence of detectable cytopathic effects at the highest concentrations tested. All glycopeptide derivatives exhibited concentration-dependent inhibition of viral replication, achieving complete suppression of plaque formation at higher concentrations. Reductions in viral RNA copy numbers were consistent with plaque assay results, confirming inhibition of productive infection.

These findings demonstrate that wild-type LLOV is susceptible to both polymerase-targeting antivirals and glycopeptide-derived compounds in a biologically relevant reservoir-derived cell model, supporting further antiviral characterization and development efforts targeting this understudied filovirus. LLOV is also suitable for experiments supporting preparedness against emerging filoviruses, specifically for testing broadly reactive antivirals.

Acknowledgement: *The work was performed within the framework of the Horizon Europe Project 101095712 OneBAT, funded by EU.*

P17

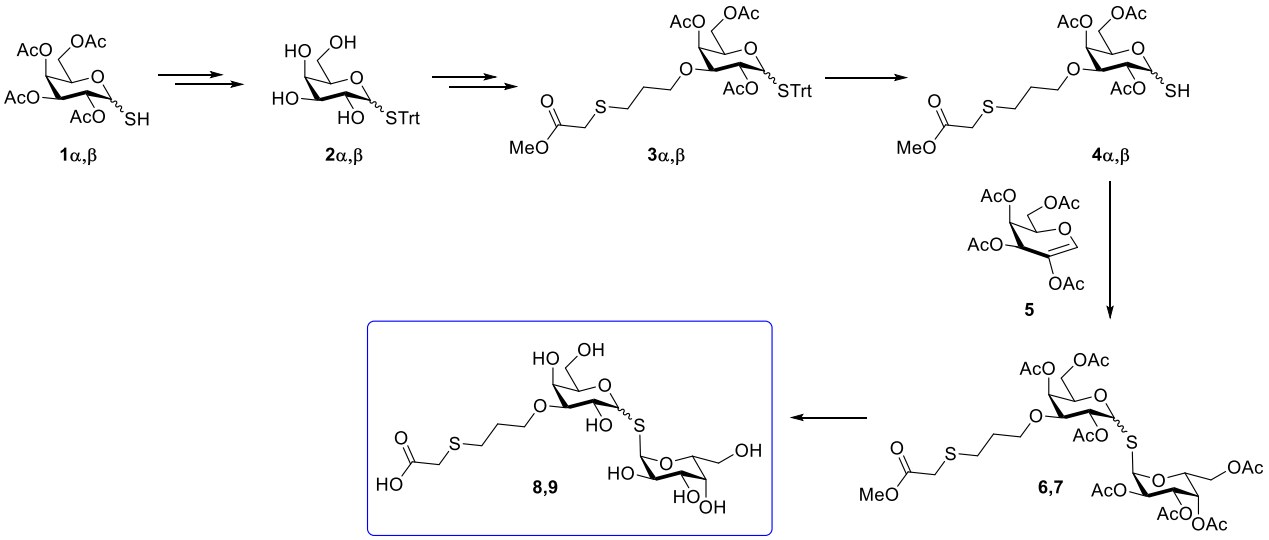
Synthesis of C-3'-substituted thiodigalactoside derivatives as potential galectin-8 inhibitors

Zsófi Püspöki,[a] Ágnes Homolya,[a] Bianka Pozsgai,[a] Anikó Borbás[a]

[a]*University of Debrecen, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, H-4032, Debrecen, Hungary*

E-mail: pzs.sofi15@gmail.com, homolya.agnes@pharm.unideb.hu

Galectins constitute a versatile family of carbohydrate binding proteins that are expressed in numerous cell types and are capable of functioning in both the intracellular and extracellular spaces. Their role in the immune system is particularly multifaceted: galectins can modulate the adaptive and innate immune responses, including by binding to carbohydrates on the surface of immune cells or by directly binding to pathogens, thereby supporting antimicrobial mechanisms [1,2].
Gal-8 is a potential drug target consisting of two nonidentical carbohydrate recognition domains (CRDs). The N-terminal domain of Gal-8 uniquely exhibits a preference for 3-sialylated galactose derivatives found in natural glycans, because of the presence of the carboxyl group [3].



Scheme 1: Synthesis of thiodigalactoside derivatives

In this study, we synthesized α,β' and α,α'-TDG derivatives (**8,9**) substituted at the C-3' position with a thioglycolic acid containing side chain, as shown in **Scheme 1**. We replaced the *O*-glycosidic bond found in compounds serving as natural disaccharide ligands for galectins with an *S*-glycosidic bond, which increases the stability of the compounds; furthermore, the carboxyl group at the C-3' position enables the interaction with Gal-8.

Acknowledgement: *The research was supported by theUniversity of Debrecen Talent Management Program (DETEP) and by the University of Debrecen Program for Scientific Publication.*

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P18

Biological effects of novel cannabigerol derivative PFD 45/I on renal cell carcinoma cells

Zsuzsanna Szabó,[a] Ali Shammas,[b] Dániel Petróczi,[c] Ilona Bereczki,[c] Anikó Borbás,[c] Árpád Tósaki,[b,d] Erzsébet Szabó,[b,d] Gábor Halmos[a]

[a1]*Department of Biopharmacy, Faculty of Pharmacy, University of Debrecen, 4002 Debrecen, Hungary*
[b]*Department of Pharamcodynamics, Faculty of Pharmacy, University of Debrecen, 4030 Debrecen, Hungary*
cDepartment of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Debrecen, 4030 Debrecen, Hungary
[d]*HUN-REN-TKI-DE Pharmamodul Research Group, University of Debrecen, 4002 Debrecen, Hungary*

E-mail: szabo.zsuzsanna@pharm.unideb.hu

Renal cell carcinoma (RCC) is one of the most common malignancies of the urinary system, accounting for approximately 90% of all kidney cancers, and its global incidence has steadily increased over recent decades [1]. RCC is frequently diagnosed at advanced or metastatic stages due to the lack of specific early symptoms, which significantly limits therapeutic success [1]. Therefore, the identification of novel compounds with improved selectivity and antitumor efficacy is of considerable importance. Cannabigerol (CBG), a non-psychoactive phytocannabinoid derived from Cannabis sativa, has demonstrated promising anticancer properties in several tumor types; however, its clinical applicability is restricted by poor aqueous solubility and limited bioavailability. Recent studies on fluorinated cannabidiol and cannabigerol derivatives demonstrated improved biological activity and pharmacological potential [2]. Eight novel CBG derivatives were synthesized and evaluated on human RCC cell lines (CAKI-2 and A498). Cell viability and proliferation were assessed using the Cell Titer-Blue assay, while long-term antiproliferative capacity was further investigated by clonogenic assay. Among the tested compounds, three derivatives exhibited significant antiproliferative activity, with PFD45/I proving to be the most potent at 30 μM. Importantly, clonogenic assay results further confirmed the inhibitory effect of PFD45/I on RCC cell survival and colony-forming ability, supporting its sustained antitumor activity. Notably, PFD45/I demonstrated low cytotoxicity in non-malignant NIH-3T3 fibroblast cells. Preliminary molecular investigations suggest that the compound may influence apoptosis- and proliferation-related signaling pathways. Western blot analysis indicated the possible involvement of the PI3K/Akt/mTOR pathway through modulation of PI3K, Akt, and phosphorylated Akt (p-Akt) expression. Previous studies have also highlighted the importance of cannabinoid-associated signaling in RCC progression and growth inhibition [3]. However, further studies are required to determine whether the observed antitumor effects are mediated primarily through CB1 or CB2 receptors, or a combination of both cannabinoid receptor pathways. Additional investigations are necessary to further characterize its biological properties, clarify precise molecular mechanism of action, and evaluate therapeutic potential in more advanced preclinical models.

Acknowledgement: *Thematic Excellence Programme (TKP2021-EGA-20) (Biotechnology) of the Ministry for Innova-tion and Technology in Hungary (G.H.). National Research, Development and Innovation Office (NKFIH-K-124719), Hungary, and HUN-REN-TKI-Office for Supported Research Groups (HUN-REN-DE Pharmamodul Research Team. The work was also supported by FK142315 program (I.B).*

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Caitriona O'Driscoll, *caitriona.odriscoll@ucc.ie*
Roland Pieters, *r.j.pieters@uu.nl*
Peter Preiser, *prpreiser@ntu.edu.sg*
Jan Weber, *jan.weber@uochb.cas.cz*
Lindomar Pena, *lindomarfiocruz@gmail.com*
Anil Chuturgoon, PhD, *chutur@ukzn.ac.za*
Jadwiga Handzlik, *j.handzlik@uj.edu.pl*
Michaela Wimmerova, *michaw@chemi.muni.cz*
Seonghun Kim, *seonghun@kribb.re.kr*
Marko Anderluh, *marko.anderluh@ffa.uni-lj.si*
Vishal Rai, *vrai@iiserb.ac.in*
Ronaldo N. de Oliveira, *ronaldo.noliveira@ufrpe.br*
Barbara Richichi, *barbara.richichi@unifi.it*
Brijesh Rathi, *brijeshrathi@hrc.du.ac.in*
Pulin K. Gupta, *guptapulin@yahoo.com*

Oral presenters

Martin Zoltner, *zoltnerm@natur.cuni.cz*
Gyula Batta, *batta@unideb.hu*
Ferenc Dániel Petróczi, *petroczi.f.daniel@pharm.unideb.hu*
Krisztina Mária Szabó, *dr.szabo.krisztina.maria@med.unideb.hu*
Ravi Durvasula, MD, *Durvasula.Ravi@mayo.edu*
Ágnes Rusznyák, *rusznyak.agnes@pharm.unideb.hu*
Miklós Vecsernyés, *vecsernyes.miklos@pharm.unideb.hu*
Beatrix Dienes, *dienes.beatrix@med.unideb.hu*
Rudolf Gesztelyi, *gesztelyi.rudolf@med.unideb.hu*
Mansi Verma, *mansiverma@hrc.du.ac.in*
Ankush Gupta, *ankushorganic@hrc.du.ac.in*
Nguyen Thi Cam Tu, *ntctupharmacy@gmail.com*
Richárd Kajtár, *kajtar.richard@pharm.unideb.hu*
Himanshi Sharma, *hsharma@hrc.du.ac.in*
Padam Raj Bhatt, *praj007@hrc.du.ac.in*
Mohammadamin Biglarikhoshmaram, *biglarikhoshmaram@mailbox.unideb.hu*

Simon Eskeif, *eskeif.simon@mailbox.unideb.hu*
Zsanett Szilágyi, *szilagyi.zsanett@pharm.unideb.hu*
Mária Fanni Boncz, *bonczmaria@gmail.com*
Bálint Lakó, *lakbalal25@gmail.com*
Boglárka Polónyi, *boglarka.polonyi@gmail.com*
Miklós Lovas, *lovas.miklos@pharm.unideb.hu*
Nawar Ahmad, *nawar.ahmad@pharm.unideb.hu*
Rasha Ghanem Kattoub, *rasha.ghanemkattoub@pharm.unideb.hu*
István Kacsir, *kacsir.istvan@science.unideb.hu*
Ágnes Homolya, *homolya.agnes@pharm.unideb.hu*
Lajos Kovács, *kovacs.lajos@med.u-szeged.hu*
István Kese, *istvan.kese@cyclolab.hu*
Zsolt Ürögi, *zsolt.urogi98@edu.bme.hu*
Viktória Goldschmidt Gőz, *viktoria.goz@ttk.elte.hu*
Dénes Páll, *pall.denes@unideb.hu*
Béla Juhász, *juhasz.bela@med.unideb.hu*
Rita Kiss, *kiss.rita@med.uneb.hu*
Zsolt Ráduly, *raduly.zsolt@med.unideb.hu*
András Szilágyi, *szilagyi.andras3@semmelweis.hu*
László Kardos, *dr.kardos.laszlo@med.unideb.hu*
Zoltán Szabó, MD, PhD, *szaboz.med@gmail.com*
Attila Bácsi, *etele@med.unideb.hu*
Eszter Lilla Tóth, *toth.eszter.lilla@med.unideb.hu*
Miklós Zrínyi, *zrinyi.miklos@unideb.hu*

Poster presenters

Alshimaa Ibrahim Zaki, *alshimaa.ibrahim@science.unideb.hu*
Balázs Nagy, *nbalu0319@gmail.com*
Barbara Nóra Balogh, *balogh.barbara@pharm.unideb.hu*
Benedek Máté Nagy, *nagybeni04@mailbox.unideb.hu*
Devesh Panchal, *devesh1444@chemistry.du.ac.in*
Dorota Lazewska, *dorota.lazewska@uj.edu.pl*
Edvin Puric, *edvin.puric@ffa.uni-lj.si*
Krisztián Zoltán Juhász, *juhasz.krisztian@anat.med.unideb.hu*
Krisztina Bodnár, *bodnar.krisztina@pharm.unideb.hu*
Krisztina Rebeka Leiner, *leiner.krisztina@pte.hu*
Muhammad Raza Saleem, *muhammadrazasaleem@mailbox.unideb.hu*
Parul Panwar, *parulpanwar@hrc.du.ac.in*
Péter Soma Szakály, *soma.szakalyvcyclolab.hu*
Samreen Saifi, *saifi.samreen@science.unideb.hu*
Shilpa, *shilpabeniwal17@gmail.com*
Zoltán Kopasz, *kopasz.zoltan@pte.hu*
Zsófi Püspöki, *pzs.sofi15@gmail.com*

Zsuzsanna Szabó, *szabo.zsuzsanna@pharm.unideb.hu*
Ram Pratap Pandey, *rp328395@gmail.com*
Bindu Tiwari, *bindutiwari8899@gmail.com*

List of participants

Agócs, Attila; Hungary
Ahmad, Nawar; Hungary
Anderluh, Marko; Slovenija
Bácsi, Attila; Hungary
Bácskay, Ildikó; Hungary
Bak, Istvan; Hungary
Balogh, Barbara Nóra; Hungary
Batta, Gyula; Hungary
Bege, Miklós; Hungary
Bereczki, Ilona; Hungary
Bhatt, Padam Raj; India
Biglarikhoshmaram, Mohammadamin; Hungary
Bodnár, Krisztina; Hungary
Bokor, Éva; Hungary
Boncz, Mária Fanni; Hungary
Borbás, Anikó; Hungary
Chuturgoon, Anil; South Africa
Czine, Péter; Hungary
De Oliveira, Ronaldo; Brazil
Demeter, Fruzsina; Hungary
Eskeif, Simon; Hungary
Fehér, Pálma; Hungary
Fenyvesi, Ferenc; Hungary
Gesztelyi, Rudolf; Hungary
Ghanem Kattoub, Rasha; Hungary
Goldschmidt Gőz, Viktória; Hungary
Gupta, Ankush; India
Handzlik, Jadwiga; Poland
Herczegh, Pál; Hungary
Hermanné Dr. Dienes, Beatrix Éva; Hungary
Homolya, Ágnes; Hungary
József, János, Hungary
Juhász, Béla; Hungary
Juhász, László; Hungary
Juhász, Zoltán Krisztián; Hungary
Juhászné Dr. Tóth, Éva; Hungary
Kacsir István; Hungary
Kajtár, Richárd; Hungary
Kardos, László; Hungary
Kese, István; Hungary
Kim, Seonghun; Korea
Kiss, Rita; Hungary
Kopasz, Zoltán; Hungary
Kovács, Lajos; Hungary
Kuczmog, Anett; Hungary
Kumar, Yogesh; India
Kun, Sándor; Hungary
Lakó, Bálint; Hungary
Łażewska, Dorota; Poland
Leiner, Krisztina; Hungary
Lekli, István; Hungary
Mező, Erika; Hungary
Nagy, Balázs; Hungary
Nagy, Benedek Máté; Hungary
Nagy, Veronika; Hungary
Nagyné Végh, Lilla; Hungary
Nguyen, Thi Cam Tu; Hungary
O'Driscoll, Caitriona; Ireland
Páll, Dénes; Hungary
Panchal, Devesh; India
Pandey, Ram Pratap; India
Panwar, Parul; India
Pena, Lindomar Jose; Brazil
Petróczi, Ferenc Dániel; Hungary
Pieters, Roland; the Netherlands
Polónyi, Boglárka; Hungary

Preiser, Peter; Singapore
Purić, Edvin; Slovenia
Püspöki, Zsófi; Hungary
Ráduly, Zsolt; Hungary
Rai, Vishal; India
Rathi, Brijesh; India
Richichi, Barbara; Italy
Rimóczi Aliz; Hungary
Rusznyák, Ágnes; Hungary
Saifi, Samreen; Hungary
Saleem, Muhammad Raza; Hungary
Sharma, Himanshi; India
Shilpa, India
Somsák, László; Hungary
Szabó, Krisztina Mária; Hungary
Szabo, Zsuzsanna; Hungary
Szakály, Péter Soma; Hungary
Szakonyi Zsolt; Hungary
Szilágyi, András; Hungary
Szilágyi, Zsanett; Hungary
Tiwari, Bindu; India
Tóth, Eszter Lilla; Hungary
Tóth, Gergely; Hungary
Ujhelyi, Zoltán; Hungary
Ürögi, Zsolt; Hungary
Vágvölgyiné Dr. Tóth, Marietta; Hungary
Váradi, Judit; Hungary
Vecsernyés, Miklós; Hungary
Verma, Mansi; India
Weber, Jan; Czech Republic
Wimmerova, Michaela; Czech Republic
Zaki, Alshimaa I.; Hungary
Zoltner, Martin; Czech Republic
Zrínyi, Miklós; Hungary